VISCERAL ANGIONEUROSES.

BY

SOLOMON SOLIS COHEN, M.D.,

Reprinted from the

New York Medical Journal
INCORPORATING THE

Philadelphia Medical Journal and
The Medical News

February 19, February 26, March 5, 1910.







(The Visceral Crises of Vasomotor Ataxia.)
By Solomon Solis Cohen, M. D.,
Philadelphia.

Professor of Clinical Medicine in Jefferson Medical College, etc.

The term visceral angioneuroses is convenient rather than exact. It is intended to imply that the manifestations of disordered function under discussion arise from circulatory disturbances rather than from primary tissue change in the organs affected, and to suggest their relationship with the familiar circulatory disturbances in the skin to which the term angioneurosis is commonly applied.

The symptomatology of the visceral angioneuroses is multiform and somewhat vague. It frequently resembles that of inflammatory or degenerative affections—sometimes that of infectious maladies-but careful analysis will usually show that there is lacking some feature essential to the diagnosis of organic lesion or of specific infection, or that the case presents a number of redundant phenomena which such diagnosis will not account for. Further, the neurovascular origin of the symptoms is usually indicated by their paroxysmal occurrence and recurrence—in crisis, as it were—while in cases of inflammation, tissue lesion, or infection the symptoms are continuous. Sometimes it happens that organic lesions or specific infections and angioneurotic phenomena coexist, and it is then quite possible, by laying undue stress upon the signs of one, to miss

^{*}Read before the Association of American Physicians, Washington, D. C., May, 1909.

the other. This error is especially to be guarded against—and in the negative as well as the positive direction—in cases suggestive of lesions demanding surgical interference, as discussed more fully in another connection.

The final element in the diagnosis, however, is the patient—his physical characteristics, his reaction to environmental change, his familial and hereditary liabilities, and his previous personal pathological his-

tory.

In a communication to the Pan-American Medical Congress of 1893 (which communication I termed "A Contribution to the Study of Idiosyncrasies") I described a class of persons in whom the vasomotor taxis is easily disturbed by influences that are without evident effect upon the majority of men, and greatly disturbed by influences that affect normal individuals but slightly—a constitutional or temperamental status to which I applied the name of vasomotor ataxia. In 1884, when my attention was first strongly directed toward the existence of this variety of the human species, patients were comparatively few, and as the condition was not described in the textbooks, I thought it uncommon. vears later, for the collective report alluded to, I had studied some 64 cases, 19 of which were reported briefly or in detail. As clinical service and other opportunities have enlarged, the cases observed have become so numerous as to induce the belief that they are much more common than any one suspects-and to put me strongly upon guard not to be misled by the personal equation. Individual report of these cases is impossible, and the leisure necessary to analyze and tabulate the great mass of records accumulated during these twenty-five

¹Vasomotor Ataxia, American Journal of the Medical Sciences, February, 1894.

years is still among things hoped for. For the present communication, dealing with visceral disturbances only, the notes of 200 cases have been reread. Space permits but a relatively limited selection to be cited, and some of these only in brief outline or perhaps with reference to but a single point of the many which each illustrates. As, however, I purpose taking up hereafter other phases of the subject, I shall place on record now a sufficiency of clinical detail to establish both affirmatively and negatively every assertion made. Attention may also be recalled to the parallel instances detailed in Allbutt's Gulstonian lectures, and in Hans Herz's monograph on vasomotor ataxia; as likewise in the reports of anomalous and aberrant cases of Graves's disease and of Raynaud's disease, the extensive bibliography of which, being embodied in various monographs and encyclopedias, needs not here be repeated.

In referring to Allbutt, it is not meant to imply that the views here expressed have that author's endorsement. In his lectures already referred to, he says, indeed, in connection with the subject of serous diarrhœa:

The diarrhoa is generally associated with other neuroses, such as migraine, cardiovascular instabilities, and the rest.
. . . The pathology of the day will attribute it, no doubt, to vasomotor disturbance and compare it with polyuria, lacrymation, and night sweats. It may be the homologue

And in his latest contribution to the subject he remarks in discussing the hæmaturia of nephralgia:

Some authors appear to find an explanation in calling

²On Visceral Neuroses, London, 1884.

³Zur Lehre von den Neurosen des peripheren Kreislaufsapparates (Ueber vasomotorische Ataxie), Berlin und Wien, 1902.

⁴T. K. Monro, Raynaud's Disease, Glasgow, 1899, and Cassirer, Vasomotorisch-trophische Neurosen, Berlin, 1901.

⁶Graefe-Saemisch Handbuch der gesamten Augenheilkunde (Zweite Auflage), Leipsig 1907, 1908.

Auflage), Leipsig, 1907, 1908. 6Op. cit., p. 85.

such hemorrhage angioneurotic, and the pain may be due to tension of the capsule in fits of vascular distention which sometimes issue in hemorrhage.

But these phrases seem intended to throw doubt upon the suggested explanation rather than to accept it.

That all visceral neuroses are of vascular mechanism is not asserted; that many, if not most of

them are, I hope to show.

Nor is the thesis here upheld that the condition of vasomotor ataxia will alone account for the phenomena described. On the contrary, they appear to have a threefold origin:

- I. A constitutional or temperamental status or liability; namely, the aberrant motility of the vasomotor system, or, rather, of that entire nervous apparatus which used to be termed "sympathetic," which Gaskell termed "visceral," and which is now known as "autonomic." This may be an actual, or only a relative imperfection; it may be manifested by excess or by defect, by undue readiness (erethism) or by sluggishness (apathism) of reaction, by want of excitability or by want of inhibition—but the general result is the same; there is a maladjustment of the circulatory relations.
- 2. An excitant; the most frequent exciting agents being (a) an endogenous or ectogenous poison—perhaps even a perverted or relatively excessive physiological product; (b) emotion; and (c) thermal change. Sometimes the excitant cannot be identified.
- 3. A local determinant, direct or reflex, which is sometimes to be recognized in mechanical and physical conditions, such as position (gravity); sometimes in circumstances that condition a local action of the excitant; sometimes in a selective drug or

⁷Allbutt and Rolleston, System of Medicine, iii, p. 408, London, 1907.

toxine effect; sometimes in a slight trauma; sometimes in eyestrain; sometimes in excessive functioning of a part with resulting hyperexcitability or exhaustion, central or peripheral. Frequently, however, it eludes detection. Local determination having once occurred, a certain tendency to repetition is set up, and frequent recurrence eventuates in morbid habit.

It has already been intimated, moreover, that under adequate excitation the same order of phenomena may occur in normal individuals; being thus, indeed, neurovascular disturbances, but not necessarily neuroses. Disturbances of the vasomotor system occur likewise as part of the essential or incidental symptomatology of various acute and chronic ailments, especially those in which a persistent toxemia is set up; but such cases are obviously excluded from the present category.

Henoch's purpura and those other rather severe syndrome groups of mingled visceral and cutaneous phenomena to which Osler has directed especial attention and the importance of which he has emphasized in a number of communications,8 doubtless bear some fundamental relationship to the group of cases here considered; and in a number of instances overlap. They are, however, in the main differentiated from the angioneuroses by their frankness, their sharpness, their relative rarity, and their probable dependence upon definite toxines, if not upon specific infections. The cases to which this paper is limited are of more common occurrence; have, in general, a more vague symptomatology a more protean variability, a less definite exciting causation; and run a more prolonged, if not always a less dangerous, course. The distinction, however, is not

⁸American Journal of the Medical Sciences, ex., p. 629, 1895; Jacobi Festschrift, 1900; American Journal of the Medical Sciences, exxvii, p. 751, 1904.

absolute. As I have previously pointed out concerning Graves's syndrome and Raynaud's syndrome, with their connecting links, so also among the more distinctly visceral types of angioneurosis, do there exist intermediate cases of many kinds and grades. It is partly for this reason that confusion still prevails in our nomenclature, and that while some physicians recognize as instances of vasomotor disorder only those which are accompanied with structural changes and functional perversions so obvious. and of such high degree, that they cannot well be ignored, others refuse to admit within the category of angioneuroses these very cases. Accurate classification and appropriate nomenclature waits upon physiological as well as pathological discovery, not only in the domain of the nervous system, but also in that of the body chemistry, and especially that of the hormones.9

Also, there remain to be solved certain questions in relation to individual syndrome groups, such as the presence or absence of infectious or toxic agents. and the identification of these, if present; the identification of the products of perverse metabolism or of increased or diminished secretory activity associated with the various symptoms, causally, incidentally, or sequentially; and the possible association of definite morphological or chemical tissue changes with definite clinical phenomena. Meanwhile, the clinical phenomena deserve more attention than they ordinarily receive—for they are not rare, but common; not infrequent angels, but almost daily visitors.

Herz distinguishes three types: (1) (Angio)-spastic, (2) (angio)ectatic, and (3) mixed; or, as I originally expressed it, syndromes dependent

The encyclopædic studies of Sajous (Internal Secretions, Philadelphia, 1903, 1907) well exhibit the vast extent and great importance of this field.

chiefly upon constriction of the vessels, syndromes dependent chiefly upon dilatation of the vessels, and syndromes in which constriction and dilatation are variously commingled. Sometimes, as was pointed out in the basic paper, such syndromes, by repetition and other influences become organized, as it were, into more or less definite and permanent associations. and we have the well known clinical pictures of Graves's disease, Raynaud's disease, Mitchell's erythromelalgia, etc.

Some observers would remove these organized syndromes from the category of ataxia, and include therein only the mixed type, which is now, I think, fully recognized. But in my own experience at least, pure spastic types are rare, and pure ectatic types are uncommon. Constrictive phenomena occur even in Graves's disease, and phenomena of dilatation even in Raynaud's disease.

That constriction is generally spastic, and that dilatation is generally paretic, while probable, is by no means certain. Dilatation of vessels may occur as well when dilator nerves are excited as when constrictor nerves are paralyzed, or even when both sets of fibres are excited or inhibited, but in unequal degree; and, similarly, constriction may result from dilator paralysis, constrictor excitation, or from unequal stimulation or unequal inhibition of both mechanisms. Our knowledge of the neurovascular mechanisms, central and peripheral, as well as of circumstances and influences which by action upon the vessel wall may bring about constriction or dilatation independently of nerve impulse, is as yet too limited to permit of dogmatism. It is for this reason that I have designated the phenomena under discussion as ataxic; for whether they

¹⁰Cf. Morton Prince, On Association Neuroses, Journal of Nervous and Mental Diseases, May, 1891.

be spastic or paretic, or both, whether they originate in the vessel wall itself or in the central or peripheral nervous apparatus, whether they result from conditions affecting dilator mechanism or constrictor mechanism, or both—and in the latter case. whether in the same direction or in opposite directions unequally—they are manifestly phenomena of incoördination. The local circulation has become unbalanced; the peripheral and central circulatory mechanisms are no longer in equilibrium; compensation is deficient, restoration is tardy. this reason, too, that recognition of the peculiarities of the individual—as expressed in physical characteristics, in reaction to certain easily applied physical, thermal, and emotional tests, and in previous history of disordered function—become so important. The diagnosis is, in the main, a diagnosis of the patient rather than of the special collocation of symptoms presented in any particular attack. attacks vary, sometimes to a surprising extent; but the individual liability remains, and may usually be recognized when looked for. Sometimes it is acquired, but usually it is congenital, and most frequently it is hereditary, being observable in many members of a family and conditions permitting, traceable throughout many generations.

The facts upon which this diagnosis may be based will be described after the illustrative cases have

been cited.

The phenomena which, lacking a better term, we describe as angioneurotic may be transient or persistent, general or local, and in the latter case they may be manifested in any tissue or in any organ; sometimes in several tissues and organs simultaneously; sometimes in one tissue or organ at one time and in another at another time. As a rule, they are both multiform and multiregional; and while

certain fundamental conditions are permanent, those which attract the patient's attention and for which he seeks relief are, in most instances, transient, and

often paroxysmal.

In the respiratory tract the best known angioneurosis is asthma. Asthma, of course, is merely the name of a symptom, the mechanism of which is varied and is not always angioneurotic. Angioneurotic asthma is of the three types, spastic, ectatic, and mixed. The differentiation of the unmixed types is at times readily accomplished by a therapeutic experiment. The injection, sometimes even the lingual administration" of the active principle of the adrenal gland relieves quickly—even though but temporarily—the ectatic paroxysm; that which has well been termed "bronchial urticaria." Such treatment, however, aggravates the spastic paroxysm; which, on the contrary, is relieved, though not with the same degree of certainty, by inhalation of amyl nitrite or injection of nitroglycerin. An indication of the constrictive or dilative nature of the attack is sometimes, but not invariably, afforded by the tension of the pulse, which is high in the spastic, and low in the ectatic variety. This, however, is manifested, as a rule, only at the inception of the attack; for later, the disturbances both of circulation and of respiration consequent upon the mechanical effect of the dyspnæa, as well as upon the accumulation of carbon dioxide in the blood, render such discrimination impossible. Also, the general tendencies of the patient's vasomotor reaction, as observed during periods of freedom, may be of assistance. when the responses of the cutaneous vessels to pressure and to heat and cold are of the ischemic variety, dyspnœa is usually aggravated by adrenalin; but when these responses are of the hyperæmic vari-

¹¹S. Solis Cohen, On Asthma, Pennsylvania Medical Journal, December, 1904.

ety, adrenalin usually relieves the asthmatic paroxysm. So, too, the patient's tendency to ischemic or to hyperæmic migraine, or the predominance, under other circumstances, of Raynaud's or of Graves's phenomena, may indicate the hypertonic or hypotonic tendency of his neurovascular mechanism. The distinction, nevertheless, is not absolute, because mixed phenomena so frequently occur, and because the same patient may at one time exhibit phenomena of hypertension and at another time those of hypotension.

The facts concerning asthma, however, are tolerably familiar. Less frequent is the recognition in practice and in literature, of the occurrence of angioneurotic phenomena in the larynx, 12 Their danger and the readiness with which their nature may be mistaken, gives them high importance. never recognized an angiospastic neurosis of the larynx, and do not know what would be its symptoms; unless, indeed, some of the curious cases of paræsthesia of that organ have such an origin. The ectatic paroxysm is, perhaps, less rare than the books indicate. I have seen recurring attacks of transient ædema of the larvnx causing intense difficulty in breathing, in a subject of tabes, in whom they were brought on by any extraordinary physical exertion, and usually passed away upon rest and spraying of the larvnx with adrenalin. In this case, which had been mistaken for one of asthma, tracheotomy was urged and declined. I later heard of the patient's death in a suffocative seizure. Here a distinct and serious organic lesion existed, to which the laryngeal paroxysms may well have been secondary; and the

¹²R. Morris gives a noteworthy picture of postmortem appearances in such a case, American Journal of the Medical Sciences, exxx, p 382, 1905. Rudolph reports a fatal case involving the trachea, Canada Lancet, March, 1904.

case is not brought forward as an instance of pure angioneurosis. The following instance, however, seems distinctly to come under that head, the laryngeal cedema being simply one of a group of angioneurotic phenomena affecting various tissues simultaneously or at different times. The case, moreover, is worthy of record because of the type of patient in whom it occurred, and because of the evident connection of the phenomena with emotional disturbances and with fatigue. The record, however, can be partial only, because, as with most of these patients, detailed history of the various and varying paroxysms during the patient's lifetime, would in itself constitute a monograph.

Case I.—Angioneurotic ædema of tongue, pharynx, and larynx; gastroenteric crises; anginoid crises. (Case of forty years' duration with adema of various parts of the body.) Miss X. Y. Z., aged fifty-two years, a member of one of the old, staid gouty Quaker families of Chester County, Pa., and as far as possible removed in ancestry and personality from those who are so flippantly termed neurotics or hypochondriacs, was one of several sisters whom the death of father and brother left without men folk, to the successful charge of an extensive farm and dairy. The patient was first seen October 14, 1899. Her complaint was of swellings coming on without apparent cause in various parts of the body, for twenty odd years. She had been free from them for the last five years, but they had returned a few weeks before she consulted me. The first symptom the patient remembered was that when a child (aged nine years) she was subject in hot weather to small red swellings, which were at first termed mosquito bites, but afterward found to have no such origin—probably hives. The details of this case of typical angioneurotic cedema are interesting and should be reported in full, but our present interest lies in the visceral accompaniments only. These are of three varieties—laryngotracheal, gastroenteric, and anginoid. In 1877 the patient was stung severely by bees. For three weeks following she was "severely swollen all over the body, could scarcely see, and was stiff in the joints." For two years after this she suffered with recurring attacks of abdominal cramp, sometimes accompanied with nausea and vomiting, sometimes

with a feeling of intense burning in the stomach, but without nausea or vomiting; or there might be profuse diarrhœa unaccompanied with pain of any kind. These attacks passed away, and she then had swelling of the lip, especially the left half of the upper lip, followed by strangling sensations, with burning and itching in the throat, which passed off and left severe headache. She would then become very sleepy. Attacks seemed to be independent of weather or of food, of occupation or of environment. The patient, needless to say, did not smoke, nor did she use alcohol, tea, or coffee. The menopause had set in when she consulted me. During the existence of the menses there was no irregularity, nor did the attacks seem to be influenced either by the occurrence or the cessation of the menses. In fact, we were unable to find any satisfactory exciting cause save emotion; that is to say, any excitement, pleasurable or otherwise. Thus, the wedding of a friend and the sickness of a sister each seemed to have been responsible for attacks which resembled angina pectoris and were so termed by the physician attending her at the time, about three years before I was consulted. The patient was very susceptible to drugs, and as she could not take what she called "allopathic" medicine, had been latterly under homeopathic treatment. Her attendant had termed her condition "heart trouble." Examination of the heart showed normal dulness, somewhat short and weak first sound, sharp aortic second sound. The radial pulse was full, moderately strong, of low tension, rate 84, intermittent on one occasion only. Swelling of the left half of the tongue came on during the examination, but subsided upon the application of adrenal powder. On November 5, 1905, the patient came to the office nearly strangling. Examination showed laryngeal ordema, which subsided upon local application of solution of suprarenalin. She stated that she had been very well under the treatment and régime formerly prescribed, un-til about six weeks previously, when she had had a swelling of the tongue, later a swelling of the thigh, then a swelling of the throat. With this latter came chilliness, stiff neck, and "the old bad symptoms." All this had followed the nursing of a sick sister. From time to time the patient reappears with the same or similar symptoms. She has no thyreoid enlargement, but exhibits the eye signs, nail signs, thermal and pressure reactions, described further on as characteristic.

I find among my records (Case II) a portion of a typewritten letter detailing a somewhat similar

series of phenomena. The signature is missing, as are also my own notes of the case; but, if my memory serves, the patient was a learned and highly emotional scholar, extremely susceptible to drug poisoning—he could not take morphine, atropine, quinine, or salicylates. To quote the written words:

The swellings, at first, always came between 2 and 3 a. m., arousing me from a sound sleep. There would be a sort of shock in the face or tongue, and then the swelling would begin. Sometimes there would be a swishing in the ears; if this was heard before I fell asleep, I knew an attack was preparing. All these attacks are attended with great depression of mind and a desire to wccp—a weary, hopeless feeling. There is a dull aching at the base of the head (brain?) and later, aching in the limbs, with an eruption of bives on the lower part of the body. The stomach is always very irritable during and after an attack. The body is rarely free from hives or blotches. Nervous shock or atmospheric changes will often bring on the swelling.

The ædema in this case affected at various times the face, the tongue, the pharynx, the larynx. It was usually unilateral (leftsided) sometimes partially bilateral. The nocturnal (or early morning) incidence of the attack is paralleled in many of the crises affecting the abdominal viscera and in the cases of muscular spasm. Pulmonary ædema is sometimes met with in similar recurrent crises. It may or may not be associated with chronic cardiac or cardiovascular affection.

That vascular disturbances similar to those observed in the tongue and pharynx of these patients not only may, but do, occur in other portions of the digestive tract has been proved by examination of a tragment of the gastric mucosa, accidentally detached during lavage,¹³ and by inspection of the appendix and bowel in several cases of abdominal sec-

¹³R. Morris, American Journal of the Medical Sciences, exxviii, p. 820, 1904.

tion cited by Osler." A few cases in which operation was done have come under my own observation and will be described briefly in the further course of this paper. These gave corroborative evidence of a negative character; that is to say, no structural lesion was found to account for the symptoms. is only through such fortuitous experiences that anatomical demonstration, positive or negative, of the soundness of the views expressed in this and

previous papers, could have been reached.

The communication to the Pan-American Medical Congress recorded the occurrence in the pharynx of blue cedema and of acute nodular distention of veins much like — although more marked — that which Barlow 15 later observed upon the hand in Ravnaud's disease. Herz¹⁶ also has observed similar phenom-The rupture of these acute varices or "blood blisters" in throat, gullet, stomach, bowel, or elsewhere, may give rise to hamorrhages, and bleeding may similarly occur from distended capillaries, or in consequence of ordinary venous congestion. Thus, blood spitting, and even vomiting of blood, occasioning a mistaken diagnosis of gastric ulcer, is not infrequent. I have recorded one such case, and have exhibited probably a dozen to my clinical classes. Section, either ante mortem or post mortem, being wanting, the absence of gastric ulcer is not con-The facts that in such cases the nutrition is well preserved, the gastric secretion not rarely subacid, and the subsequent and previous history of the patient full of angioneurotic phenomena of various kinds; together with the further fact that the patients go on for long periods without any serious danger to life arising (as in cases which I have observed for periods ranging from two to twenty

 ¹⁴Osler, *Ibidem*, exxvii, pp. 751 et seq., 1904.
 ¹⁵See Monro, *op. cit.*, p. 83.
 ¹⁶Op. cit., p. 54.

years), would seem, however, to be strong negative evidence. Some of these patients, of course, have passed out of observation, and their fate cannot be stated. In one case the patient is known to have died in an attack resembling cerebral hæmorrhage, and in another, in which sudden death occurred, the attending physician made a diagnosis of angina pectoris.

Hæmorrhages of all kinds are, indeed, quite common in the subjects of vasomotor ataxia. Stress was laid upon this fact in my original communication, and I shall return to its consideration later.

The disturbances of the stomach and intestines not attended with bleeding, are much more common than those just alluded to. Their variety is, if not infinite, at least indeterminate. Allbutt relates many instances; I described some illustrative cases in my first communication; Herz records a number; and nearly every writer upon Graves's disease or Quincke's ædema cites them as among the complications of these syndromes. In the present communication I shall instance only a few, associated with other interesting phenomena illustrating the personal and hereditary liabilities of the patient.

Case III.—Goître, with asthma; paroxysmal tachycardia; hay fever; emaciation; paroxysmal polyuria (apparently hyperacid); gastric crises; subacidity; possible tuberculosis. Miss X. Y. Z., aged thirty-six years, of American birth and English ancestry, was referred to me by a colleague on October 17, 1907. She had been sick for three years. Following an attack of bronchopneumonia there had remained more or less persistent dyspnæa and spasmodic cough without expectoration. After two or three months, attacks of paroxysmal orthopnæa with wheezing and autopalpable fremitus had developed. With these came on likewise flatulent indigestion with borborygmi, pyrosis, and paroxysmal epigastric burning. The patient rapidly emaciated. From time to time there would be days of frequent, almost incessant, micturition, the urine being profuse and pale. The asthmatic paroxysms became more frequent. At the

beginning of an attack the face became pallid, the heart began to beat rapidly, and pulsation could be heard in the ears. The patient chilled easily, and was at one time inclined to attribute the attacks to cold, but it had become evident that they were independent of weather, climate, food, or exertion. They were frequently, however, excited by emotion, especially if she was startled or angered. For three years in succession, before the development of the present condition, the patient had suffered with autumnal hay fever while in England, but since the onset of the existing syndrome she had not suffered from nasal or ocular irritation, except when she smelled coal gas, which excited

sneezing, coryza, and lacrimation.

The patient's heart, at the first examination, was feeble in action, the first sound short, the second sound sharp; the pulse regular, frequent (108), and full; the arteries hard, but not sclerotic; the tension high (140 mm. systo-The lungs were over resonant; respiration being harsh with numerous sonorous and sibilant rales. hands were cyanotic and showed the nail signs. graphy and factitious urticaria were readily developed. There was no history of angioneurotic ædema of the skin or of the visible mucous membranes. There was goitre, but none of the eve signs except dilatation of the pupils. But two examinations of the gastric contents were permitted; both showed subacidity. The urine occasionally contained albumin, cylindroids, and red cells. Tubercle bacilli could not be found in the sputum. The tuberculin tests were not permitted.

The patient's father was aged and healthy. The mother had goitre and the eye signs, but no exophthalmos and no tachycardia. She was distinctly gouty. A maternal aunt

had typical Graves's disease.

CASE IV.—Paroxysmal epigastric pain or abdominal cramps; marked eye signs; no goître; occasional palpitation; transient pigmentations; acrocyanosis; local syncope. Miss X. Y. Z., aged twenty-four years, a seamstress, of Austrian birth and Hebrew race, was short, stout, and well nourished. She had fair skin, with dark hair and eyes. For some time a sudden, sharp, burning pain in the epigastrium had come on at irregular intervals, usually while the patient was at work, and might recur several times a day. At times it radiated toward the left side of the chest; at times the pain in the thorax preceded that in the epigastrium; sometimes there was "a bruised feeling" in the side, and abdominal cramp without epigastric pain, which,

however, would be provoked if food was taken within an Occasionally there was nausea and faintness, but never vomiting. As the attack passed off, there might be considerable eructation, but the patient did not at other times have either belching or flatulence. There was no There was no pyrosis and no blood spitting. The bowels moved regularly twice a day. The appetite was not affected by the pain, but the patient usually refrained from eating, because experience had shown it to be unwise to take food at that time. Examination of the gastric contents showed nothing abnormal. There was no tenderness upon pressure, and no abdominal lesion of any kind could be de-The menses were regular, but for the last two years, during which time these attacks had developed, the flow was at times very slight; and if she attempted to work during the catamenial period, severe abdominal cramps were experienced; otherwise there was no disturbance.

The patient was an orphan, an only child, and no information concerning her family was obtainable. She never suffered from headache. In conversation she exhibited frequent spontancous retraction of the upper eyelids, sometimes retraction of the lower lids as well. Graefe's sign was wanting. The forehead wrinkled perfectly. The pupils were equal and normal and there was no tremor of the closed lids. There was no tremor of the hands. skin of the hands exhibited slight duskiness, which ran out upon elevation. She said that at times the hands became white and numb. She had not observed any connection between these attacks and the attacks of pain. There was red dermography. Hives did not occur. The patient frequently, upon arising in the morning, found yellow spots upon the face and chest, which itched intensely and passed away in the course of ten or twenty minutes. The finger nails showed a red base, a blanched centre, and a deep red terminal loop. The pulse was 84, soft, equable, and of low tension; systolic pressure, 110; diastolic, 78. Palpitation of the heart frequently occurred, especially if the patient was startled or excited. She was then unable to walk or work. If she rested, the paroxysm passed over quickly. Precordial dulness was not increased. The apex beat was in the fifth interspace, parasternal line; the first sound of the heart was empty; both second sounds were weak. There was a soft, basic systolic murmur at midsternum and at the third left interspace. Hæmoglobin was 85; red corpuscles, about 4,000,000; white corpuscles, 7,000. urine showed no abnormality. The thyreoid gland was not

enlarged. The patient was not hysterical; prior to the onset of the symptoms related she had had a severe emotional strain.

Case V.—Paroxysmal nausea; local cyanosis (of hands and nose); eye sign; nail signs; tuberculous and gouty family history. Mrs. A. B. C., aged twenty years, of American birth and English ancestry, had been married for some months, but had never missed a menstrual period. Prior and subsequent to marriage she had had attacks of "sick stomach" unaccompanied with pain or headache. They came on, as a rule, about half an hour after eating, at any time of day, and most frequently after the evening meal and when the day had been one of excitement or fatigue. The character of the meal appeared to be unimpor-She never vomited. Sometimes there was cructation of odorless, tasteless gas, which gave partial relief, and although there was no sense of distention, the patient felt that further belching would relieve. There was no flatulence, no pyrosis, no sense of weight, no other discomfort than nausea. The attack subsided spontaneously in from fifteen to forty-five minutes and very quickly when a small dose (1/200 grain, 1/3 milligramme) of nitroglycerin was swallowed. The bowels were regular. The urine was normal. The patient had always been "nervous." She laughed and cried readily, but rarely had hysterical at-When she was nauseated, the cheeks burned but did not become flushed. In cold weather the finger nails and the tip of the nose became slate blue. At other times the finger nails were blue, yellow, and red, with terminal red loop. The feet might be cold in hot weather. There was deficient expansion of the left apex, with impaired resonance and feeble breathing. The heart was feeble; there was no murmur; the pulse was regular, full. So in rate, of low tension (110). The hæmoglobin was 80; the red cells, about 4,000,000; white cells, 7.500. There was quick, red dermog-The pupils were dilated equally, the lids were tremulous, the commissure widened on fixation. thyreoid gland was full, but not notably enlarged. was no tenderness in the epigastrium. No anomaly of gastric secretion was shown by test meals. No abdominal lesion could be found. The father's family was tuberculous, the mother's family was gouty. Lately the patient had been overusing her eyes, without glasses (she was myopic), and the attacks were more frequent. She had also been subjected to a prolonged emotional strain.

thyreoid enlargement; bicolored nails; eye signs. Mrs. X., a Russian Jewess, aged thirty years, had suffered with abdominal cramps off and on for two years. They might be first referred to the umbilicus or to the epigastrium. sometimes to the right iliac fossa. They usually spread over the whole abdomen and to the back, and might be either preceded or followed by neuralgic pain referred to the precordium. The attack lasted an hour or two, and might recur daily or even twice in a day, or there might be a free interval of several weeks. Following the attack there was anorexia. The taking of food appeared to have no influence, as the attacks might come on before eating, immediately after eating, or a long time after eating. There was no palpitation, no fainting, and no vertigo. The pulse was of low tension. The nails showed a central pallid zone and deep red terminal loop. Both upper lids and lower lids were retracted, the retraction becoming more evident during the excitement of conversation or upon application of the fixation test. The pupils were not dilated. There was slight thyreoid enlargement. This patient was constipated, but the attacks were only partially relieved by the continuous use of purgatives and enemas. No organic lesion of any kind could be demonstrated. There was no menstrual trouble.

CASE VII.—Hyperacid gastric crises; epistaxis; hay fever in substitution for astivoautumnal diarrhaa; nail signs; dermography; hives; nocturnal muscular spasm; angioneurotic famliy history. Mr. A., aged about fifty years, of American birth, German ancestry, Hebrew race, a man of mobile emotions, but not at all hysterical, rather of more than ordinary self control—had been subject since childhood to paroxysms characterized by burning pain in the epigastrium, accompanied with a sense of faintness and some-times with nausea, but rarely with vomiting. If during the attack it was possible to expel by the throat and mouth the gas that seemed, from the sense of distention, to accumulate in the œsophagus, partial relief was experienced. It was ejected in a series of explosive gusts something like hiccoughs, and was tasteless and odorless. Sometimes there was expulsion of gas from the bowel at the same time, and this was also usually odorless. The attacks varied much in severity. The most distressing feature of a severe paroxysm was the intermittent regurgitation from the stomach into the mouth of a thin, clear, colorless, highly acid, and sometimes very bitter fluid. This was ejected in small quantities, from one to two or three teaspoonfuls,

and at intervals varying from one to ten minutes. times the fluid seemed to rise into the middle portion of the esophagus, but the power to expel it was lacking, and as it fell back into the stomach the burning pain which seemed to be concentrated in the subxyphoid region was much increased. The attacks were now comparatively infrequent, and a year or two might pass without one; but formerly they had recurred three or four times in a year. Their severity had also lessened in the last ten years. At first they might occur at any time of day. For some twenty years they had been nocturnal only, frequently awaking the patient from an untroubled sleep. He attributed them to overwork or excitement or anxiety. On two occasions only—when cheese had been eaten at the evening meal was there any apparent connection between the paroxysm and the taking of food; and the patient believed these to have been simply coincidences. The burning might last, with remissions, during the whole of the night, or it might pass off in an hour or two. During the period of frequency and severity the pain could be much mitigated or entirely relieved by the application of a mustard plaster over the epigastrium. Latterly this did not seem to have been necessary. The burning could also be measurably relieved by the sipping of ice water or by taking sodium bicarbonate dissolved in hot water. Frequently, as the epigastric distress disappeared, there would be sudden, sharp, perhaps repeated discharges of an acrid fluid from the bowel. The stools at this time would sometimes contain strings of mucus, rarely small lumps of fecal matter. Apart from these crises, the patient had no gastroenteric disturbance; appetite and digestion were always good; nutrition was well preserved, and the bowels functionated regularly and satisfactorily. As a child and young man, the patient was subject to what was called "dysentery" in the months of August and September; that is to say, abdominal cramp would occur suddenly and would be followed for a week or two by frequent, liquid, and sometimes blood stained stools. These attacks ceased abruptly if untreated, and quickly if treated by evacuation of the bowel and the administration of paregoric. They were independent of food, weather, or exertion. The last one occurred in the patient's nineteenth year. The following spring he suffered for the first time from hay fever, which had recurred annually since and could only be avoided by going to the seashore. The patient had no nasal abnormity, and no enlargement of the thyreoid gland. He did not exhibit any

of the eye signs. His nails were tapering, pale pink, longitudinally ridged, and exhibited a deep terminal crescent. He exhibited but slight dermography. Factitious urticaria and pilomotor reflex were absent. He had hives occasionally. Headaches, from which he began to suffer when he entered college, were relieved by glasses, and now seldom occur. He had myopia, astigmatism, and now presbyopia. There was no abnormality of the eye ground. Occasionally (seven or eight times in the course of his life) he had had very brief attacks of objective vertigo, preceded by momentary dimness of vision, and accompanied or followed by high pitched tinnitus aurium. The ears were normal and the hearing was exceedingly acute. patient was putting on flesh and was a little winded on walking rapidly or climbing stairs, but the arteries were soft; the heart and lungs were normal; the pulse was slow (rate 60) and of low tension (110 systolic). There were a number of minute cutaneous angiomata. As a child, the patient was subject to bleeding from the nose, especially upon exertion, such as running a race. He was occasionally —at long intervals—wakened from sleep by a subjective sound as of a pistol shot, and with this his arms and legs would be violently thrown out, to quote his words, "as with an electric shock." The muscular movement might occur without the sound.

His family history was traceable throughout many generations and branches, and on the father's side exhibited nothing significant. On the maternal side, vasomotor neuroses were frequent, one or another of the following conditions being exhibited by one or another maternal aunt, uncle, or cousin, as well as by the patient's brothers and sisters: hay fever; asthma; angioneurotic œdema; quinine, opium, and strychnine idiosyncrasies; migraine; paroxysmal tachycardia; pseudorenal colic; pseudoappendicitis; erythema nodosum; erythema exudativum; leucoderma; Graves's disease; chorea; neurasthenia. Diabetes mellitus and gout were also found in the maternal line. A cousin had (chronic) glancoma. There was no epilepsy in the family so far as known.

These cases should be sufficient to illustrate the great variety in the symptomatology of the gastroenteric crises; their variability in the matter of gastric secretion; and their association with the family tendencies and individual constitutional signs, to be described more at length hereafter.

In a number of other cases more or less resembling those narrated, a somewhat more definite exciting causation has been observed. Thus (Case VIII), one man, who is a subject of leukoderma, and bleeds freely from very slight hæmorrhoids (a relative of Mr. A. of Case VII), has found that the paroxysms from which he suffered — vertigo and nausea, with gray or pallid face, cold perspiration, intense umbilical colic, and sometimes syncope were brought about by eating yeal; and has prevented their recurrence by regulating his diet accordingly. A woman (Case IX) with marked eye signs, and formerly subject to migraine, declares that pyrosis is always provoked by taking quinine or any "strong medicine"; but she also suffers from nocturnal crises similar to those described in Case VI, without definite exciting cause. A physician of middle age (Case X) found that his attacks of serous diarrhea were provoked by driving in a cold wind; and prevented them by wearing a woolen abdominal bandage and wrapping himself up in a fur robe. Among the cases included in the series of records consulted for this paper, are, however, several of serous diarrhœa of paroxysmal recurrence over a series of years, in some of which sanguinolent discharges have also been observed from time to time, and for which no definite exciting cause, either in diet or weather, could be detected. In a number of the patients, however, especially women —and, curiously, six out of ten of these are nurses —the attacks seemed to follow prolonged fatigue or severe emotional strain.

In previous communications I have recorded two cases of membranous enteritis, and the present series contains ten additional instances, of which four are in men and six in women.

In all of the cases thus briefly alluded to, a suffi-

cient number of the individual characteristics and of the angioneurotic associations are present to warrant their inclusion in the present discussion. A single case may briefly be cited. This particular one is chosen because it illustrates, in addition to the diarrhæa, a possible connection of this disturbance with epilepsy, and also calls attention to the peculiar cutaneous reaction to silver exhibited by quite a number of these patients.

CASE XI.—Serous diarrhaa; headache; palpitation; abdominal cramps; transient unconsciousness without mus-cular spasms; acrocyanosis from cold; dermography; nail sign; black silver (sulphide?) line. J. J., aged thirty-three years, for ten days had had pain in the back and limbs, followed by diarrhoa. For five years he had been subject to these attacks at irregular intervals, and independent of weather or food. The stools were frequent, painless, watery containing neither blood nor mucus. He might have cramps at times, in warm weather only, but without looseness of the bowels. He had typhoid fever at the age of eighteen, but the diarrhea did not follow until ten years later. Widal and von Pirquet reactions were negative and the stools did not show either typhoid or tubercle bacilli (Rosenberger). At night he was often troubled with headaches, which usually began in the occiput and traveled to the vertex. According to the patient's statement, a swelling "as thick as his finger," took place along this track. When the pain thus began in the back of the head, it affected both sides simultaneously. Sometimes it began in the temple on the right side and radiated to the nose. He had throbbing of the heart at times, accompanied by "weak spells" and dimness of vision. This sometimes lasted for half an hour. At times he became dizzy for a moment and lost consciousness. The nails were slightly curved, their general color a leaden blue, with a distinct white band in the centre, and red bands above and below. He perspired freely even in winter, but endured winter better than summer. The finger ends, however, turned blue in cold weather, and the feet were always cold, summer and winter. The ears and nose did not get cold. He never had hives or any other eruption. The track of a silver probe drawn along the face was marked by a black line, provided the perspiration had first been removed. An aluminum probe excited

red dermography. No organic lesion of any kind could be detected. There is no record concerning the eyes.

Hepatic crises occurred in but four of the 200 cases forming the basis of this paper. Two of the patients were women and two were men. In all the symptomatology of gallstone colic was closely simulated, except that jaundice was slight or absent. In two of the women and one of the men the absence not only of calculi, but of any organic lesion whatsoever, was demonstrated by operation. Only one of these patients was under my care at the time of the operation, but I have verified the history of the others. The case in which exploratory incision was made at my instance will be discussed farther on in connection with other surgical cases,

Case XII.—Patient operated upon for hepatic colic, nothing found; cardiac palpitation; epistaxis; hæmoptysis; bleeding hæmorrhoids; eye signs; nail signs. Mr. Y., aged thirty-eight years, a tailor, of Hebrew race, born in Russia, suffered with umbilical pain occurring paroxysmally, and apparently induced by fatigue, anger, or excessive smoking. Some years previously an operation had been undertaken for cholelithiasis, but no lesion had been found. His skin was dusky; he had telangiectases and angiomata; exhibited dermography, factitious urticaria, and spontaneous retraction of both upper and lower eyelids. He had had epistaxis and hæmoptysis, but exhibited no sign either of tuberculosis or of gastric ulcer. He occasionally passed blood by the bowel, which he attributed to hæmorrhoids. He had occasional attacks of palpitation of the heart, but no cardiac lesion was to be detected, and there was no enlargement of the thyreoid gland. His nails were noted as "characteristic." There was no evidence of pancreatic lesion.

CASE XIII.—Hepatic colic; operation; no lesion; eye signs, nail signs, dermography, etc. Mrs. Z., aged forty years, of American birth, German parentage, had been operated upon for hepatic colic and no lesion found. She now had paroxysms of cardiac palpitation and epigastric burning, with belching and water brash. She showed eye signs and nail signs, dermography, and factitious urticaria; as a child she had had frequent bleeding from the nose.

CASE XIV .- Hepatic (?) colic; no evidence of gallstone;

umbilical cramp; intermittent claudication; eye signs; nail signs. Mr. R., aged forty years, of Austrian birth and parentage. Hebrew race, insurance solicitor, complained of pain in the right hypochondrium, occurring paroxysmally, sometimes radiating to the epigastrium, sometimes to the back and to the right shoulder; sometimes it run down the flank and might even follow the course of the ureter. At times there was cramp in the umbilical region, when the hypochondrium was not affected. The pain was always of sudden onset and sudden departure. It was sharp and of short duration, but might sometimes last from fifteen minutes to half an hour. It usually occurred an hour or two after eating, but might occur at times when the stomach was empty. Sometimes it was followed by sharp pain in the region of the right nipple; and pain in the right or left breast, sudden and stabbing, might occur independently of the hypochondriac colic. The patient's complexion was sallow but he had never been jaundiced, though he thought that on one occasion his eychalls were yellow. At times the pain was accompanied with nausea, but never with vomiting or diarrhea. He was usually constipated. He never suffered from indigestion. The attacks usually came on in the fall of the year, and might recur daily or sevcral times a day, or once in two or three days, over a period varying from two weeks to a month. Constipation usually became worse at this time unless purgatives were taken, but he might at other times go for several days without a stool and yet not suffer an attack; nor did persistent purgation relieve it during this period. He had consulted several physicians both in America and in Europe, had visited Carlsbad and other watering places on both sides of the Atlantic, and had had all sorts of "cures." He had asked a European and an American surgeon to operate upon him, and they had both refused. All his medical advisers had suspected gallstone, but they had all failed to verify the diagnosis. When I first saw him I thought I felt induration in the gallbladder region. There was tenderness at this point; the right rectus was rigid; the liver was enlarged downward. Following rest in bed, brisk calomel and saline purging, and broth diet, the induration and hepatic enlargement disappeared and the rigidity of the right rectus muscle relaxed. The tenderness: and the tendency to colic, however, remained for some: time. The patient was also subject to cramp in the right lcg, which came on suddenly, whether at rest or walking. This patient showed the scleral exposure on the fixation

test; localized pilomotor reflex with sluggish red dermography; a fringe of telangiectases along both costal borders, with considerable dilatation of superficial venules elsewhere in the thorax and in the dorsal region. The abdominal veins were not distended. The pupils were dilated; the thyreoid gland was slightly enlarged; the nails were of a general slate blue color with deep red base and terminal red loop; the hands when dependent were cyanotic; the color ran out upon elevation. The heart was weak; with feeble first sound, short second sound, and a hæmic basal Hæmoglobin was 74; red blood cells, about 4,-000,000; white blood cells, 6,000. The urine occasionally showed albumin, no casts, no bile. Indican was usually high and the sulphate ratio altered. The Cammidge reaction was absent. On two occasions, shadow erythrocytes were found. The fæces were apparently normal. The lungs were normal. The liver and spleen were not permanently enlarged. The patient's mother and her sister died of consumption; his father of heart disease; his half sisters and half brothers, born of another mother, had, to quote his own language, "stomach trouble and all kinds of troubles." I have counselled exploratory incision, but in view of the previous declination of surgeons to operate, the patient is, as yet, unwilling.

Renal disturbances are more common than almost any other variety except the gastroenteric, and they may be associated with actual renal lesions, thus complicating the diagnosis. In view, however, of their long continuance, of the paroxysmal recurrence of symptoms, and of the exhibition of other crises, gastroenteric cardiac, respiratory, or cerebral, by the same patients, it seems justifiable to conclude that the permanent affection of the kidney, finally set up, is secondary to the continued disturbance of circulation and nutrition. In ninetveight of the 200 case records examined for this paper, there is a note of transient albuminuria; and in twenty-five there is mention of red blood cells or of shadow cells in the urine. In my first series of sixtvfour cases, albumin and blood cells were found in the urine at some time, in more than half; and I am inclined to the belief that sufficiently frequent examinations would greatly increase the proportion of cases in which this condition is found.

Still more convincing as to the angioneurotic character of the renal paroxysms is the case about to be narrated. Severe renal symptoms initiated a series of typical Graves's phenomena, in a woman whose mother and child also exhibit characteristic signs of vasomotor ataxia; but for nearly three years there has been no recurrence of renal phenomena, and frequent examinations of the urine reveal only occasionally a trace of albumin or a few shadow cells; while the patient has steadily put on flesh and recovered her full strength.

CASE XV.—Typical Graves's syndrome, following suppression of urine with fever and delirium; recovery; hives; scanty perspiration; dilated pupils; intermittent ptosis; frequent retraction of upper lids; epistaxis; tremor; dermography; purpura; nail signs; mitral regurgitation. Mrs. X., aged thirty-one years, of American birth and German descent, following an attack of bronchitis with apparently pleuritic pain in the right side, had suppression of urine, with dry skin, fever, oppression in breathing, rapid and feeble action of the heart, headache, and slight delirium. I saw her two days later, in consultation. Under the treatment already instituted, secretion of urine had been resumed, and the urine was found to contain a moderate quantity of albumin, with very few casts and a few blood The most evident sign upon casual inspection as the patient lay in bed was the flushed face and the retraction of the upper lids. The pulse was of low tension, full, weak, and rapid. There was a faint systolic murmur. The pupils were dilated; there was fine tremor of the hands; dermography was intense; the eye lid "hitch" was readily elicited; but the thyreoid gland was not enlarged. I saw the patient again two months later. This time there was marked exophthalmos and considerable bilateral enlargement of the thyreoid gland. The pulse was 140. That the diagnosis of Grave's syndrome previously made was correct, was now quite evident. The urine was normal in quantity and quality, and has so continued during the thirty months that have elapsed since that time. Under

treatment, the exophthalmos has disappeared, although retraction of the lids is still exhibited upon fixation, and sometimes spontaneous retraction under excitement. patient exhibited dermography and tricolored nails, and had been subject to hives since childhood. She always felt very uncomfortable in hot weather, and attributes this to the fact that she did not perspire freely. She stated that when hurried, worried, or startled, she used to feel what she described as an "inward tremor," and if the excitement was long continued, would tremble violently all over the When she was fourteen or fifteen years of age her eyes had become very sensitive to light, but the pupils would not contract, and for that reason she had had to wear dark. glasses. This phenomenon had accompanied the onset of menstruation and had passed off in a year or two. As a baby she had had ice cold hands and feet and had not perspired except under the arms, where at times the sweating was profuse and fœtid. This continued well into wom-She had had bleeding hæmorrhoids, and as a child had been subject without provocation to bleeding from the nose, which was always profuse and difficult to stop. Even now she bled readily from a slight cut, and the bleeding was sometimes difficult to check. Menstruation was usually profuse and painful. For some months after the goître first subsided, it tended to reappear with the menstrual flow. For the last eight months this has not occurred. On several occasions the patient has exhibited "bruises" of unknown origin and twice an extensive purpuric eruption; once on the chest and arms; once on the lower extremities. She has been married for some years and has a child four and one half years old. Shortly after childbirth she noted on the right thigh a soft mass, which has within the last twelve months enlarged rapidly. It is probably a lipoma. Three or four times I noticed a drooping of the right upper eyelid at the outer canthus. This was temporary only. The patient stated that it was first noticed after a fall in childhood, and recurred from time to time when she was tired and run down. This lid retracts at other times, in unison with the left upper lid. The heart murmur has been growing steadily louder and more pronounced, but symptoms referable to cardiac incompetency have not developed.

Incidentally, it may be remarked that in the treatment of Mrs. X. the tremor of the hands and arms, which had become very troublesome, disappeared under the administration of parathyreoid substance; and that the patient pro-

fesses herself most comfortable when taking pituitary substance. I use a special preparation of the infundibular lobe, which has also been useful in other cases of Graves's

disease under my carc.

The mother of this patient exhibited intermittent ptosis, also of the right upper eyelid. She was gouty, and had incipient cataract in both eyes. Her left upper eyelid was retracted when the fixation test was applied; sometimes the right upper lid also; the pupils were dilated, but in view of the opacities of the lens, this was perhaps without special significance. She had dermography, was a bleeder as a child, and still bled quite readily from slight causes. She had tricolored nails.

The patient's son (aged four and one half years) had appendicular crises, exhibited dermography and the terminal red line upon his pink nails. He frequently passed uric

acid gravel, but otherwise appeared to be healthy.

The coincidence of angioneurotic visceral crises and an actual lesion of one of the organs concerned, which, however, is insufficient to account for the entire symptomatology, is illustrated by the following cases:

CASE XVI.—Floating kidney, with renal and other crises; operation; kidney enlarged, capsule adherent; eye signs; nail signs; crythema; circumscript adema; palpitation; syncope; hemiparæsthesia; gastralgia. Mrs. Q., aged twenty-three years, of American birth and German and English ancestry, was subject to headaches; was said to have had scarlet fever at six years of age, and following this, "kidney disease" and "heart trouble." She had had a miscarriage about six months before consulting me. For three or four years she had noticed intermittent swelling of the fect. Recently the left leg had been affected. There had been frequent attacks of palpitation of the heart. She was conscious at times of a missed beat. The attack would frequently be followed by syncope. For ten days she had been having intermittent swelling of the feet and passing bloody urine. She had had hæmaturic attacks accompanied with severe abdominal pain twice before—eight years and three years previously—and this continued intermittently for about three months each time. It was independent of the menstrual period, and bore no apparent relation thereto. The menses were regular; before marriage, every three weeks; since the miscarriage, every four weeks. The urine

showed a small quantity of albumin, a few hyaline casts and cylindroids, and a number of red blood cells. An enlarged and displaced right kidney was discovered upon ex-The lungs and heart were normal. Operation was done by Senn's method. The kidney when exposed was found to be enlarged, much congested, and the capsule too much thickened and adherent to be removed. surgeon, however, incised it in a number of places. covery was uneventful. The patient began to put on weight and improved greatly for a number of months. Headaches then began to be frequent and troublesome. With these came attacks of drowsiness, abdominal cramps, pains about the waist, nervous attacks in which the patient had causeless fears; hallucinations; swellings in various parts of the body; rashes of various parts of the body; occasional attacks of causeless vomiting. Although she was wearing glasses, I requested Dr. George M. Gould to go over the refraction. He found compound hyperopic astigmatism, and the new lenses he ordered relieved a great many of these symptoms-more especially the headache, which has not since returned. The patient continues however, from time to time, to have various abdominal crises. This is not due to nephroptosis, for the kidney remains in place. In addition, there are from time to time attacks of transient numbness of one arm or of the entire side; "choking spells," one of which lasted about two hours; hæmaturia and hæmoglobinuria; "heaviness" of the heart; coldness of the legs. Sometimes a red ring appears across the nose, one inch from the end, "which has a bruised appearance" (I am quoting the patient's description.) The same "bruised appearance" has occurred at times under the eyes. Sometimes in such attacks the eyes are "The lips are red, the rest of the body a lifestaring. less white." (This is the husband's description.) patient is not hysterical. She exhibits the characteristic cye signs and cutaneous reactions of vasomotor ataxia. The nails are filbert shaped, pink, ridged, and with a deep red crescent at the tip. The urine at times shows casts and albumin, at times albumin without casts. at times neither casts nor albumin; at times red blood cells or shadow cells, at times white blood cells; sometimes hæmoglobin without blood. There has never been any characterestic inorganic material. The quantity of urine is usually between 1,200 and 1,600 c.c. per diem. Indican, urea, chlorides, sulphates, and phosphates are about normal. At present the patient's principal complaint is of what

used to be termed "gastralgia." Skiagraphy demonstrates the absence of ptosis. Nutrition is good, and it is difficult to consider the case an instance of ordinary chronic nephritis.

In view of the well known tendency to hæmorrhagic phenomena in chronic nephritis, the following case is not beyond question; yet the varied and peculiar character of the crises is strongly suggestive of angioneurotic origin:

CASE XVII.—Gastroenteric crises; chronic nephritis with hamaturia and crises simulating renal calculus; skiagram negative; no crystals found in the urine; eye signs; nail signs; dermography. W. B., aged forty-four years, Canadian birth, German ancestry; gardener; had consulted many physicians and many hospitals, and his case had been variously diagnosticated as "alcoholic gastritis," "myocarditis," "acute nephritis," "chronic parenchymatous nephritis with exacerbations," "renal calculus," "Dietl's crisis in floating kidncy," "vesical hæmorrhage," "renal hæmorrhage," and plain "hæmaturia," without topical or causative qualification.

The family history as obtained gave nothing important. The personal history included diphtheria, measles, whooping cough, scarlatina at eighteen, typhoid fever at nineteen, rheumatic fever at thirty-nine. A congenital branchial fistula was imperfectly closed by operation when the patient was twenty-two years of age. Ten years ago internal

hæmorrhoids were removed by operation.

This man confessed to an excessive use of alcohol until six months before coming under observation. For about a year previous to that he had had frequent paroxysms of abdominal pain, usually epigastric or umbilical, often accompanied with vomiting, sometimes recurring eight or nine times daily, and always independent of food or drink. The paroxysms might be weeks or only days apart, and might last one day or longer. This ceased and was followed by paroxysmal pain on both sides of the back in the kidney region, extending forward and down the flanks. In the intervals there were attacks of headache, usually paroxysmal and sometimes one sided. Both headache and lumbar pain were preceded by constipation, the relief of which was followed by amelioration of the other symptoms. Five or six weeks before applying to the Out Patient Department of Jefferson Hospital he had had an attack termed

"grippe," the symptoms being described as chills, fever, and pain in the knee, with general muscular soreness. Later. the legs, feet, and left arm, wrist, and hand became red and swollen, but without pain. The face and neck were swollen, but not discolored. Later they became shiny, pale, and cold. This attack lasted about six days. Micturition became frequent, and was accompanied by general tremor. Sleep was disturbed by bad dreams. The then began to suffer again from colicky pains in the ureteral region, and passed bloody urine for several days. When seen shortly after this there was slight pretibial œdema, albuminuria, but no hæmaturia and no casts or crystals in the urine. Nine months later he complained of sharp, stabbing præcordial pains and a return of the nephralgic symptoms, which alternated with vertigo and drowsiness. The urine, which had been free, became scanty. The kidney was not palpable; the spleen was not palpable; no enlargement of the liver was detected. The heart was rapid, the first sound almost inaudible, being replaced by a soft systolic murmur; the second pulmonic sound was accentuated; blood pressure was 105 systolic, 75 diastolic; the pulse was regular and rhythmic. The patient exhibited the characteristic eye signs, nail signs, and dermography. The eyegrounds were normal. There was no thyreoid enlargement. Close watching in the hospital failed to find any distinct evidence of renal calculus or swelling of the kidney and no ureteral clots were found in the urine, which, however, frequently contained free blood, albumin. hyaline, and hyalogranular casts. Cystoscopic examination revealed no lesion of the bladder and no stone in the bladder. The blood came from both kidneys. Several skiagraphic examinations failed to show renal or ureteral calculus.

Among women who exhibit the phenomena of vasomotor ataxia, whether visceral or cutaneous, menstrual disorders are quite common; but whether the proportion of such disturbances exceeds that among women in general I am not prepared to say. The association of menstrual disorders with Graves's disease is, of course, well known, and this forms another point of contact between the organized and recognized syndrome and the cases of irregular symptomatology. In many of the cases actual le-

sions are present; in some, sufficient to require op-Nevertheless, operation rarely relieves all the symptoms, and this perhaps would justify the opinion that some, at least, of the uteroovarian disturbances are, like the other symptoms presented by such patients, angioneurotic. The point of particular importance is this, that while the uterine disorder, displacement, or lesion ought to receive attention and, if necessary, surgical, mechanical, or medicinal treatment, it is not to be looked upon as the source of all the symptoms. It may be, according to its degree or kind, one of the determinants or of the expressions of vasomotor disorder, or a result of the intermittent circulatory alteration, together with the accompanying disturbances of tissue tension and nutrition, to which Herz has called attention. This observer finds involved not infrequent. and in long standing cases does not hesitate to consider them the results or sequels of vasomotor ataxia. In some of my own cases such associations have been found, though I can place my hands upon the records of but two cases of invoma, and was not, before reading Herz, inclined to regard this as more than incidental. Displacements (versions, flexions), however, are fairly common, both in the young and the old, the single and the married: as are also chronic congestions and enlargements. Several of my patients have been treated surgically for the relief of the uterine lesions, and while this has gotten rid of a certain portion of the symptoms, there have always remained outstanding others clearly vasomotor in origin. Sometimes the angioneurotic symptoms first attract the patient's attention after a gynæcological operation; and their almost normal occurrence during the climacteric is well known.

[&]quot;Two marked instances and others less marked occur in the present series.

Two cases out of the 20 exhibiting marked uterine disturbances may here be cited, and some are cited in other connections (e. g., Cases XX, XXI, XXII, XXIV, XXV, XXVII, XXVIII, XXXII, XXXVI,

etc.).

CASE XVIII.—Metrorrhagia; urticaria; erythema; hyperidrosis; glycosuric crisis; eye signs; dermography; nail signs. Hemophilia, gout, and diabetes in family. An obese unmarried woman, aged thirty-eight years, of American birth, German and English ancestry, was referred to me in 1904. Her father had been diabetic and gouty and was said to be subject to "bruises of the leg" and "erysipelas" (probably erythema or eczema). The patient's menses were never regular. In 1886 she was said to have ovarian neuralgia, and was later curetted. In 1894 she suffered with "nervous prostration" following a severe emotional crisis. Upon recovery she nursed a sick brother, and then her mother, who died of uterine carcinoma. After this the "nervous troubles" returned. Rest cure was instituted, and she began to get obese. In 1896 she sprained her ankle. While lying in bed uterine næmorrhages developed. The 'menses flowed without cessation" for ten to fifteen days at a time, and then there would be reduced flow, or freedom, for seven or eight days. There was frequent, violent cramp. The condition lasted three or four months, closing with a second curettement. It returned. A second gynæcologist amputated the cervix for supposed malignancy. Metrorrhagia continued, however, and the third gynæcologist diagnosticated "flabby uterus" and packed. After rest treatment the flow stopped for a while and migraine, abdominal pain, and serous diarrhoa supervened. When I saw the patient there was a continuous uterine oozing with irregular fits of flooding. The womb was large and flabby. Under medicinal and hygienic treatment the oozing ceased, but the flooding continued, although with lessening severity and frequency, until about two years ago. Apparently a sort of menopause is now setting in; in the last six months there has been only twice a slight flow. The patient laughs, cries, blushes or gets angry, with slight provocation. At one time she was subject to hives and to dietetic erythema. She stands hot weather badly. At times she has nocturnal attacks of "dry throat," followed by profuse salivation, and in the morning a "general rash" is seen, which lasts from two to twenty-four hours. There is no heart or lung lesion. The pulse varies in rate from

85 to 90; is full, regular, of low tension. The urine collected by catheter occasionally contains albumin, blood cells, cylindroids, urates, oxalates; never distinct casts. The blood is normal as to hæmoglobin and cell counts. The upper eyelids retract spontaneously and on the fixation test; the pupils are dilated; there is a complex refractive error. Goître is absent. Dermography is elicited, the uails are tricolored. The hands and feet are always red, remaining warm and perspiring in winter. After attacks of pain the head and neck perspire freely; sometimes the perspiration has a bad odor. The patient's maternal grandfather was a bleeder, dying of apoplexy. Her paternal grandfather suffered with dry skin, "winter itch," and facial neuralgia. He died in old age of "heart disease."

While this paper is going through the press a glycosuric crisis has developed in this patient, following physical fatigue while in the mountains. The first sign was polyuria, 3000 to 4000 c.c. of colorless fluid being passed. Pruritus vulvæ with swelling and an eczematoid condition of the labia and contiguous parts followed, but sugar did not appear in the urine until five days later, three days after her return to the city. The quantity of urine fell to about 2000 c.c., and glucose varied from I to 2.5 per cent. by fermentation test. Milk diet was instituted. Three days later the urine reduced copper and bismuth but did not ferment with yeast. Pentose tests were not carried out, and since then neither reduction nor fermentation has been found, although milk sugar, glucose, and pentose-rich fruits were given and full mixed diet restored. Was there a disturbance of pancreatic circulation?

CASE XIX.—Ovarian neuralgia; painful menorrhagia; hay fever; paroxysmal acrocyanosis; relaxation of uterine ligaments; operation; substitutive crises; thyreoid enlargement; eye signs; nail signs; anidrosis. Mrs. P., aged thirty-five years, of American birth, mixed Irish and German ancestry, had autumnal hay fever for seventeen years. She showed eye signs and nail signs. Her hands became greenish white in cold weather, the nose cold and red. Nevertheless, she felt more comfortable than in summer, because she could not perspire. She was nervous and frightened easily. Under excitement the heart palpitated, she became pale, the limbs became chilly, and she felt as if insects were crawling over the body. She always blushed easily; frequently dark red spots appeared on the cheeks or on one cheek without known cause: one ear

would frequently burn. She was subject to abdominal cramps, without nausea or vomiting, but associated with pain in the ovarian region. She sometimes had leucorrheea, Menstruation was irregular, painful, and profuse. There was considerable dragging and pain in the back. A gynecologist called in consultation found the womb enlarged and retroverted, the ovaries tender and enlarged, and, upon performing abdominal section, found both of them to contain small cysts, sufficient to justify resection. The relaxed uterme ligaments were also shortened. While the operation gave relief to other symptoms, the patient continued to have abdominal cramps, and diarrhea became substituted for the leucorrhea. This woman has considerable enlargement of the thyreoid gland; there is no palpitation of the heart except when startled. She frequently feels pulsations in her limbs, which she thought were the motions of her bloodvessels, but they are distinct muscular waves, such as are frequently observed in neurasthenic persons.

Crises of cardiovascular disorder sometimes assume the most prominent place in the symptomatology of visceral angioneurosis, either temporarily or permanently. The vascular and pseudovascular throbbings of neurasthenics and the common throbbing of the abdominal aorta are familiar; but in the cases of angioneurotic disorder the throbbing may involve any part of the aorta, and any of its branches, to such an extent as closely to simulate aneurysm in the region affected. This was notably shown in the following instances:

Case XX.—Arterial throbbing simulating thoracic ancurysm in a case exhibiting gastroenteric crises, dermography, factitious urticaria, cpistaxis, cyc signs, and nail signs. A very intelligent, highly educated woman, aged forty-five years, occupying an important position in the teaching world, was frequently roused from sleep by violent palpitation of the heart and shortness of breath, which condition would internit and recur for several hours. Later it began to come on while she was in the cars going to and from school, or even while she was teaching. Whiskey administered on one or two of these occasions increased the difficulty, as did also aromatic spirit of ammonia. Sodium bromide, also taken as a domestic prescription, at

first gave relief, but later was without effect. A friend for whom she sent to give her massage noticed persistent throbbing beneath the sternum and some swelling of the neck, and told her that she had "aneurysm." A physician was summoned and confirmed this opinion; but a consultant diagnosticated "exophthalmic goitre." I found a broad, full neck, but no enlargement of the thyreoid gland. Dermographism and factitious urticaria were easily produced; telangiectases and characteristic eye signs and nail signs were found. Inquiry elicited a history of gastroenteric crises of various kinds, and frequent attacks of The patient had, of course, been causeless trembling. treated by various physicians for indigestion and for gout. She belonged, indeed, to a gouty family, and herself possessed Heberden's nodes. She had a malposition of the uterus, which was relieved mechanically, and a high degree of refractive error—compound myopic astigmatism with presbyopic diminution of accommodation and anisometro-While under observation she had several attacks of epistaxis, preceded by intense headache, injection of the eyes, and a throbbing pain in the back of the neck, which symptoms disappeared upon the onset of bleeding from the The arteries were hard—not sclerosed—and the pulse of high tension. Symptoms were measurably relieved by nitroglycerin and by correction of the refractive error, and still further relieved by the rest treatment later instituted. There was no cardiac lesion, and an x ray picture showed merely a slight dilatation of the aorta.

CASE XXI.—Arterial throbbing simulating abdominal aneurysm; pseudorenal colic; eye signs; nail signs; dermography. Miss A., aged thirty years, of American birth and parentage. German and English ancestry, a teacher, not hysterical, complained of violent throbbing in the abdomen. She had noticed a swelling and there was thrill and bruit. She was subject to abdominal crises resembling renal colic. The x-ray picture showed no aneurysm, and no stone in the kidney or the ureter; and although blood was found in the urine occasionally, it did not at any time show crystals. The patient exhibited the characteristic eye and nail signs and cutaneous reactions of vasomotor ataxia, and after treatment has been free from attacks for five years.

Throbbing in the rectum is an unpleasant symptom sometimes experienced. It may be accompanied with or preceded by sudden stabbing pain, and followed by bleeding or the appearance of an external

pile. It is, however, marked and frequent in a gouty, neurotic woman, aged sixty-two years (Case XXII), who has no hæmorrhoids, but who used to have attacks termed "dysentery"—that is to say, abdominal cramps, with sanguinolent mucous discharges.

CASE XXII.—She has dilatation of the left pupil, with intermittent retraction of the left upper eyelid; but no lesion of the fundus, no goitre and no cardiac disorder. There is no sign of tabes or of nephritis. The finger joints are typically gouty and enlarged, but also the tissues about them swell and subside—a circumscript ædema. She has transient flushings of the pharynx, and was said to have had croup—probably an attack of laryngeal ædema. There is gout on one side and tuberculosis on the other, in the French and English ancestry.

Reference of pain to the heart, that is, to the præcordial region, or region of the manubrium sterni, is quite common. In some cases the diagnosis of pseudoangina is clear; in other cases it is difficult to exclude true angina pectoris, and, indeed, in the further progress of the case this condition develops; but in many cases the pains are not anginoid in character. They are variously described as burning, stabbing, shooting, pressing, and sometimes the patient is unable to give any clear description. The pain may be associated with palpitation, more often with a sensation of sinking, and sometimes is actually followed by syncope. I shall recur to this subject in another connection.

In the case of a patient who afterward died in coma following a second attack of hemiplegia, and, therefore, presumably of cerebral hæmorrhage—the pain started in the midclavicular line of the second interspace to the left and ran over the shoulder, but not down the arm. It was experienced only when first going into the street from the house, and, according to the patient's statement,

would become so severe after walking two or three squares that she was compelled to stop and rest, after which she could go on all day without recurrence of the pain. This symptom disappeared about two years before the fatal termination.

The case was one that had begun as asthma, attended with profuse sweating, scanty urination, and albuminuria; later, polyuria; which symptoms disappeared before the others developed. In this case also there was a malposition of the uterus, and operative rectification without relief to other than local symptoms. (See Case XXVIII.)

lief to other than local symptoms. (See Case XXVIII.) Case XXIII.—Pseudoangina in a patient exhibiting the characteristic phenomena of vasomotor ataxia. W. M., aged nineteen, farmer, of Russian birth, Hebrew race, was suddenly seized, while at work in the field, three months before coming under observation, with sharp, shooting, præcordial pain and palpitation of the heart. Apparently there was momentary apnæa, and the patient had a sense of impending death. This passed quickly but dyspnæa and pain continued for about an hour. Other, shorter, and less severe attacks followed on the same day, and he had not been free from them for a day since. Their frequency was increasing, and often there were as many as twelve in a single day. There were occasional pains around the neighborhood of the apex beat, of a sharp, shooting character, radiating to and down both arms, especially the left, but not attended with the same distress as those first described. Paroxysms were more frequent after full meals, especially at night; he seldom passed a night without being awakened by pain. The patient was constipated, and had frequent cructations of sour gases.

His cheeks were flushed and the superficial venules were dilated. Fifteen to twenty seconds after exposure to the air of the room, the skin of the chest showed a general mottling or marbling, or irregular pink areas appeared, about the size of a shilling, in some places arranged in alternation with equal blanched areas. There was quick, red dermography, but no factitious urticaria. Skin reflexes were exaggerated in general; the pilomotor reflex was quick and extensive. If one hand was immersed in ice water, its fellow became red, and then bluish purple, in from three to five minutes. If the hand was immersed in lukewarm water, it reddened, but there was no change in the other hand. Very hot water produced in both hands

the same appearance as very cold water. The nails were tricolored; the terminal red band was narrow but well defined; the proximal blue band was broad. (On another occasion the nails were pink with deep red terminal loop.) The hands would sweat profusely in hot weather, and reddish patches similar to those described appeared over the arms and trunk. Sometimes the patches were dead white, surrounded by a red areola. He flushed easily, when resting as well as during exertion, and the ears, or one ear, would frequently burn and become hery red. Eyes: The pupils were equal, moderately dilated, excessively mobile, and responded readily to light, accommodation, and convergence. The lids were decidedly tremulous when lightly closed. The sclera was exposed above the cornea on applying the fixation test. The sclerotics were pearly, the cornea clear, and the conjunctive pale. The retinal vessels were injected. There was low compound hyperopic astigmatism. The lungs were normal. Heart: The apex impulse was visible and palpable in the fifth interspace in the parasternal line. More forcible pulsations were present in the fourth interspace and third interspace just to the left of the sternum. There was no thrill. Cardiac dulness was normal. At the apex the first sound was lacking in good muscular tone. It was decidedly murmurish. The second sound was snappy. The aortic element of the second sound was loudly accentuated. The first sound was barely audible at the aortic cartilage. The second pulmonic sound was relatively accentuated. During his stay in the hospital, the patient complained of pain starting in the abdomen, usually around the umbilicus, and traveling in divers directions. On one of these occasions a distinct cystolic murmur was heard over the aortic cartilage and in the vessels of the neck. The first sound at the apex was obscure. The thyreoid gland was slightly enlarged. There were a few pigmented spots along the back, but angiomata and telangiectases could not be found. The pulse was rapid, irregular, quick, receding, of low volume and tension. The tracing showed a normal venous pulse, arterial pulse of low tension, apex beat quick and unsustained. Blood pressure on three occasions registered: During quiescence, systolic, 125; diastolic, 75. During quiescence, systolic, 130; diastolic, 80. During paroxysm, systolic, 115; diastolic, 85.

The patient was well nourished and appeared to be intelligent. His manner was restless; he rested comfortably in bed, flat on his back, except during the paroxysms, when he felt more comfortable sitting or bending forward. His

voice was high pitched and husky. Nose and throat: There was deflection of the septum. S shaped, to the right anteriorly. The pharynx was injected. There was no swelling around the laryngeal region. The vocal bands exhibited slight muscular weakness in approximation, and injection at the bases. The urine was usually of high specific gravity, highly acid, occasionally showing traces of albumin, but no sugar. The urea was normal, indican was high; there were no casts, no crystals, but occasional erythrocytes. The blood was normal. The faces contained neither ova nor parasites. There was no occult blood; tubercle bacilli were not found. The gastric contents, after test breakfast, showed a total acidity of 0.2336 per cent., or 64 acid grade; free hydrochloric acid of 0.1314 per cent., or 36 acid grade; combined acids, 0.1314 per cent., or 30 acid grade. Lactic acid and lactic acid bacilli were absent. There was a trace of blood, and yeasts were present.

The patient stated that the family was "not nervous."

The patient stated that the family was "not nervous." One brother was subject to apparently spontaneous epistaxis; the mother and another brother to sick headache.

The father was healthy.

Hamorrhages are frequent, and frequently lead to mistaken diagnosis. They may occur anywhere, from the retina to the fundament. Epistaxis not dependent on nasal lesion is the most frequent form, but retinal hæmorrhage, hæmoptysis, hæmatemesis, hæmaturia, menorrhagia and metrorrhagia are not uncommon. I have recorded a few cases in my previous series, and Monro cites quite a number in association with Raynaud's phenomena. Herz includes hæmorrhoids as among the phenomena attributable in some cases vasomotor ataxia. I have numerous instances among my records, but was inclined to regard the lesion as a coincidence. Intestinal bleeding may occur in the absence of hæmorrhoids. The diagnosis of angioneurotic hæmorrhage rests upon exclusion of sufficient organic, toxic, or traumatic cause, and recognition of the patient's constitutional characteristics. In the case (XVI) of floating kidney with hæmorrhagic crises, the attacks of bleeding became

less frequent, but did not cease after the successful operation. Several of the uterine cases exhibit excessive and irregular bleeding. In this connection I may cite, without reporting in detail, the cases of a mother and daughter that exhibit many instructive points; also a case of hæmoptysis and a case of retinal hæmorrhage.

CASE XXIV.-Metrorrhagia in a woman of hamophilic and gouty family; migraine; eye signs; nail signs; dermography. Mrs. X., of American birth and parentage, English ancestry; aged forty-five years; was not my patient. She accompanied her daughter, and I obtained her history. From childhood she had suffered with migraine, and from puberty with menorrhagia and metrorrhagia. A displaced kidney had been operated upon, and some ovarian disease or disorder had also necessitated operation, but of its nature I was not informed. It was not suppurative. She knew herself to be a "bleeder," and to be of a bleeding family, and at both operations there had been considerable difficulty in stanching the blood. A maternal uncle had died of hæmorrhage, supposed to be from the trachea, following a slight blow. She was under the impression that the administration of thyreoid extract had helped to control her metrorrhagia. She had occasional tachycardia; there was no heart lesion, and the thyreoid gland was normal to palpation. She exhibited spontaneous widening of the commissure and nearly constant dilatation of the pupils; the nails were characteristically tricolored; there was quick red dermography, and the patient was subject to frequent burning and redness of the face, often of one cheek only. The family history on both sides was gouty.

CASE XXV.—"Nervous heart"; hæmoptysis; angiocctasis of tongue, pharynx, and epiglottis; enlarged thyreoid gland; early pulmonary tuberculosis; chlorosis; dermography; nail signs; menstrual irregularity; hæmophilic and gouty family history. Miss X., aged twenty-one years, daughter of the patient just described and of a tuberculous father, now dead, had been treated three years before coming under my observation for "nervous heart." She menstruated once at twelve years. There was no return of the flow for four years, and then it came on irregularly, but painlessly and never profusely, at periods of six or seven weeks. She always had much headache around the fourth week and became highly nervous until

after the discharge. A gynæcologist who was consulted found no pelvic lesion. A little more than a year ago she began to feel "run down," to cough, and to spit blood. As a child she had occasional attacks of bleeding of the nose and blood spitting, but no attention was paid to these symptoms. She did not bleed easily from scratches, and adenoids were removed during her childhood without notable hæmorrhage. She showed pilomotor reflex, dermography, and tricolored nails, but no eye signs, except dilatation of the pupils. The thyreoid gland was slightly enlarged. She was subject to hives from hot weather or excitement; the only edibles that she had been able to incriminate were pears and tomatoes. Her maternal grandmother did not eat fish, as distressing hives were likely to follow. The patient felt hot every morning and would sweat profusely, but her general temperature did not appear to be elevated at any time if the thermometric record can be depended upon. She felt worse in summer than in winter, and coughed less on cold days than on warm ones. The tonsils and the glands at the base of the tongue were much enlarged, and the latter were covered with distended veins. The epiglottis was covered with a network of dilated ves-The larynx appeared to be normal. Enlarged and tortuous veins covered the pharyngeal wall and the pillars of the fauces. Both apices were excessively resonant; otherwise percussion of the chest showed no abnormality. There was a fine crackling at the left apex anteriorly, and at the upper portion of both lungs posteriorly. Præcordial dulness was normal; the cardiac apex was normally situated and both sounds of the heart were normal at the apex. A soft, systolic murmur was heard over the base on both sides, and there was a faint venous hum in the neck. Hæmoglobin was 65 per cent., red cells nearly 4,000,ooo. There was very little expectoration, and examination of the infrequent sputa showed neither blood nor tubercle The response to the Moro test was pronounced. The urine contained a slight quantity of albumin, a few red blood cells; no sugar, no crystals.

CASE XXVI.—Old retinal hamorrhages in a patient showing the signs of vasomotor ataxia and without discoverable visceral or hemic lesion. Miss F. F. complained of bleeding from the nose, frequent micturition, burning after passing water, pain across the shoulder, dizziness and "rush of blood" to the head. Nothing abnormal was found in the urine. The second sound of the heart was accentuated, the first sound was short and rather feeble. The

pulse was soft and of low tension, rate 84. Hæmoglobin was 75 per cent. red cells proportional; leucocytes normal. The spleen was not enlarged. There was a venous hum. Dermography was present. The nails and the hands showed the typical signs. The thyreoid gland was somewhat enlarged. The commissure widened on fixation of the eyeballs. She was not conscious of any difficulty of vision. The marks of old retinal hæmorrhages were found.

CASE XXVII.—Hæmoptysis (from trachea or bronchi?); enlarged thyreoid gland; pigmentation; anginoid pain; occasional tachycardia; circumscript ædema with erythema and venous congestion; choreic movements. E. X., aged twenty-two years, the daughter of a tuberculous mother, was referred from a town in the interior of Pennsylvania. For three weeks she had been spitting blood, bright red and frothy. The quantity was small. There was no cough until the blood was felt in the throat. The lungs were normal. She had been well until five years ago, when she thought she caught cold, and attributed a stoppage of menstruation to this cause. Since then she had never been regular; the periods were painful and the flow scanty. The attending physician had found no uterine or ovarian lesion, and this finding was confirmed by a gynecologist of national repute. There was indigestion and some constipation. At times the feet swelled. Burning of the cheeks, at first paroxysmal, had become a constant symptom, and frequently the face swelled considerably, always in the morning. It was painful, and often discolored over a circumscribed area on each side; the color was at first pink, then purple or blue. The burning sensation also extended to an area over the back of the neck and to a spot in the throat over the trachea, causing the patient to make frequent efforts to clear the throat. Bloodspitting first followed such an effort. No local source of hamorrhage was seen in the pharynx or larynx. This patient exhibited a peculiar deep brown, almost black, pigmentation about the eyes, involving both the upper and lower lids and extending almost to the evebrows above and to the cheeks below. At times she complained of thoracic pain, simulating angina. The heart was irregular, the pulse rate reaching at times 140, and sometimes slowing down to 80 or 90. Micturition was frequent, but the urine normal. This patient had an enlarged thyreoid gland. She was said to be nervous and easily frightened.

Paroxysms of choreic movements frequently accompanied the menstrual periods.

The hæmorrhagic tendency is shown also by the purpuric or ecchymotic spots which occur apparently spontaneously (possibly from intoxication) and from very slight physical force, scarcely to be called trauma, as when a child knocks against a chair. Certain unfounded accusations of cruelty to children have been based upon formidable looking bruises thus innocently originating. I would emphasize this point as of great significance in medical jurisprudence. Granted an angioneurotic crisis with fatal termination and a cadaver exhibiting apparent bruises, and sufficient ground exists for an accusation of murder, especially in the case of a stepchild! Yet the physician who testifies truthfully for the defense under such circumstances may have to contend not only with the incredulity of court and jury, but also with the uninstructed scepticism of his professional brethren. I have personally observed one case, in which a moderate parental chastisement (no doubt deserved) was followed by black and blue discoloration and swelling of the buttocks, sufficiently alarming in appearance to cause the physician to be sent for. Both the child and the father exhibit the personal signs of vasomotor ataxia. The father was subject to gastric crises (provoked usually by the eating of cheese or veal that did not affect others), the recurrence of which has been averted by regulating his diet. Other members of the father's family exhibit various angioneurotic phenomena. I have seen purpura, sometimes recurrent, and the bruiselike spots in all types and varieties of cases and subjects—the Raynaud group, the Graves group, the visceral groups, and the various vaguer groups.

In connection with the frequency of hæmorrhages,

I may recall attention to the fact that venous congestion, instead of appearing as a general cyanosis, is sometimes sufficient to produce distinct local varices, which may be intermittent or permanent, and even venous hæmatomata—blood blisters—which may become ruptured spontaneously or through deliberate or accidental force.

My first series included three cases in which these blood blisters were seen in the pharynx. In one, the patient gave a history of two attacks of suffocation; relief on one occasion coming through spontaneous bleeding from the throat, and on the other through bleeding deliberately induced by digital

pressure.

In another case, in addition to the pharyngeal varices, the uvula and posterior pillar of the fauces were the seat of a cyanotic cedema, in association with urticaria of the fundament and angioneurotic The patient, who ædema of one half of the face. had many and various angioneurotic paroxysms, was one of a gouty, neurotic, diabetic family, and her brother, sisters, and daughter likewise exhibited interesting vasomotor phenomena. She died, at the age of seventy, twelve years after the attack reported, in coma which was apparently apoplectic, and following the sudden onset of hemiplegia and aphasia. Autopsy was not permitted, and whether there was rupture of a cerebral aneurysm, arterial oozing, bleeding from sinuses or a serous effusion, cannot be affirmed. In any event, I cannot separate the death from the long and consistent history of vasomotor disturbance. Another of my patients, a woman aged forty-eight years, died in a similar manner, after a protracted paralytic attack with apparent recovery and relapse. Herz has made analogous observations. While it is true that angiospastic cerebral crises may give rise to paralytic

phenomena, sometimes quite severe, the possibility of apoplexy as a terminal event in vasomotor ataxia

is also to be considered most seriously.

In the older woman there had been no notable arteriosclerosis, and the family is long lived and not apoplectic. In the younger woman (Case XXVIII) there had been for several years distinct and increasing arterial degeneration, with the peculiar anginoid symptoms already described (see reference

on page 423).

CASE XXVIII.—Her earlier medical history has been placed on record elsewhere in illustration of the effect of adrenal preparations in controlling asthma. In addition to her paroxysms of dypsnœa, she had polyuria, hyperidrosis, gastric crises, suppression of urine, hæmaturia, intermittent albuminuria, and finally, I have no doubt, nephritis as well as endarteritis. Autopsy was not permitted. tient's mother was a hemiplegic; had several retinal hæmorrhages; was subject to venous engorgements of the tongue; and died in uræmic coma. Her younger sister has had hemianopsia and retinal hæmorrhages and was one of the patients operated upon for abdominal crises simulating appendicitis. Her elder sister, who exhibits Heberden's nodes on two or three fingers, has paroxysms resembling hay fever (angioneurotic ædema of the nasal passages), which, however, do not occur at definite periods of the year.

As to the death under discussion, there is no certainty that the lesion was hæmorrhagic; it could have been due to thrombosis. The question has arisen in my mind as to whether the treatment with adrenal substance—which had, however, been long discontinued, the symptoms which suggested it having disappeared—could have had any part in inducing the arterial lesions which this patient manifested for several years before her death. That vasomotor ataxia, more especially the spastic type, itself plays a great part in the development of arteriosclerosis there can be little doubt. The constant disturbance of the circulatory balance and the consequent nu-

tritional disorders of the vessel walls are sufficient to bring this about. They also render the patient more liable to the ill effects of ordinary exciting causes. I have under care several cases of arteriosclerosis with angiospastic cerebral crises, and an

early history of migraine.

But there may be cerebral hæmorrhage without sclerosis of the arteries. Several of my "vasomotor" patients are subject to frequent recurrence of headache, with or without vomiting, accompanied with pain in the neck, tumultuous, forcible action of the heart, high tension of the pulse, flushing of the face, and intense conjunctival injection. Dr. Howard F. Hansell has examined some of these cases and found, at such times, overfilling of the retinal vessels—arteries, or veins, or both—and cupping, leeching, or venesection, or the use of aconite or veratum viride, with hot applications to the feet and cold applications to the head, usually brings about recovery from the attack. The patients know, now, not to delay when the symptoms are urgent; and the prompt domestic use of the pharmacal and thermal measures indicated, sometimes averts the necessity for bloodletting. But suppose that in such persons the condition should go on for several days unrecognized and untreated—hæmorrhage, paralysis, and perhaps death, might readily result.

It is in connection with cerebral disturbances in general that the greatest difficulties in the diagnosis of angioneurosis of an organ arise. Circumscript cedema, localized ischæmia, localized congestion, are all conceivable, and even demonstrated conditions of the brain. That the attacks of nausea with syncope and without vomiting, which have for convenience been described among gastric crises, are in reality cerebral, is highly probable. That some of the vomiting is cerebral is not improbable. That

headache, vertigo, and migraine are cerebral is certain. Transient visual disturbances, including partial vision, hemianopsia and even complete blindness, are not uncommon; and among a number of cerebral crises, which I hope to report in full at some other time, are two cases of transient aphasia. The subject of angioneurotic disturbance of the brain is however, too big to be discussed here, and I must content myself with calling attention to its many possibilities.

DIAGNOSIS.

The manifestations of vasomotor ataxia are divisible into many groups, classes and subclasses which, however, may be assembled fairly well under the following heads: A, general; B, local or regional, and, C, multiregional (but not general).

In each of these the mechanism may be:

I. Constrictive (usually, but not necessarily, spastic). This may show in the skin as blanching (ischæmia) or as cyanosis of various shades and tints (venule capillary congestion), as the venous or arterial system is predominantly affected.

2. Dilative or hyperæmic. This is not necessarily parctic, but may be either active or passive, either capillary or venous. It is shown cutaneously by

flushing, or by cyanosis, or by œdema.

3. Mixed, in which dilatation and constriction of vessels are found in the same patient at the same time; sometimes in the same region, sometimes in different regions. This is the most common form. Its cutaneous manifestaion may be cyanosis, mottling, or alterations or comminglings of blanchings and varied colors, or ædema.

In many cases predominately constrictive, minor phenomena of dilatation may occur permanently, or may recur regularly or occasionally; and likewise in most cases predominantly hyperæmic, minor

phenomena of constriction may at some time be manifested. Hence, strictly speaking, nearly all cases are mixed. But the threefold division is warranted by the facts 1, that pure types of the extremes do occur; and 2, that one or the other extreme may so far predominate as to render the other by comparison insignificant.

All these phenomena (constrictive, dilative, mixed) have been seen in the eye grounds and in the throat, as well as in the skin; and it is fairly to be presumed that they occur in the same way in

regions inaccessible to view.

Any of these varieties may be paroxysmal or nonparoxysmal; of brief, protracted, or indefinite duration. Usually some manifestations are permanent, or at least persistent, others paroxysmal. They may be of frequent or infrequent recurrence, and either apparently periodic or irregular in time. Usually after frequent and protracted recurrence the phenomena, even if not originally persistent, become to some extent permanent; and, when the patient suffers from acute or chronic disease of any kind, the vasomotor disturbances will enter into its symptomatology, in which they may be dominant or of comparatively minor importance. Pain is usually a significant feature of the paroxysmal attacks; sometimes it is persistent, but in many cases it is slight, infrequent, or even absent.

The diagnosis of visceral angioneurosis rests first, of course, upon the exclusion of primary infectious malady or structural lesion in a case the symptoms of which exhibit a paroxysmal character or tendency, and are reasonably explicable upon the theory of disorderly vascular action; second, upon the recognition in the individual patient of certain physical characteristics and certain reactions to environmental change; and third, upon the pathogenic ten-

dencies exhibited in the patient's personal or family history.

The physical characteristics and the significant reactions to environment are not, indeed, all present in all cases; nor in any one case are they likely to be all present at the same time; nor does the same individual always present exactly the same phenomena. They are less evident, as a rule, in children and aged persons than in adolescents and young They vary greatly in degree, not only in different patients, but in the same patient under different circumstances; and among the factors tending to lessen their intensity is the hygienic treatment appropriate to the condition. Nevertheless, a sufficient number of these signs will be found in each patient, at one time or another, to permit the diagnosis to be made with reasonable assurance. They were described in my previous communications and for convenience they may here be repeated under the following headings: Skin, finger nails; eyes; thyreoid gland; heart and vessels; muscular movements. Certain of the phenomena referred to under one heading may again be alluded to under another the cutaneous signs, for example, being largely vascular; chiefly various and varying forms of capillary or venous congestion; less frequently, blanching.

Skin. In many cases, and more frequently in children than in adults, the superficial cutaneous vessels of some portion of the body will be dilated in such a way as to give to the skin a marbled or mottled appearance. which can usually be intensified by local cold and diminished by local heat, stroking, or pressure. Sometimes local heat causes a uniform reddening. Cold weather intensifies and warm weather usually lessens the mottling. It may be concentrated or diffuse, minute or extensive in area, and be situated upon the upper portion of the body only,

or upon the lower portion only, or upon both. It is usually bilateral and symmetrical, but sometimes unilateral; it may be confined to one or two extremities, or to the chest, back, or abdomen only, or involve the whole trunk, or occupy any combination of regions. More common is a deeper and more massive congestion affecting the hands, which may be permanent or recurrent. Occasionally it is intense, but most frequently it is slight, except under stress of cold weather or when artificially intensified by the application of cold. The hands may be of uniform tint, in various shades of pink, red, purple, or blue, or they may exhibit varied combinations and interminglings. Usually the color runs out upon elevation of the limb; and upon resumption of the natural hanging position, returns first as a general pink hue, thence passing into the purple and blue tints. In such instances, there is, obvious ly, a passive dilatation of the terminal capillaries and venules. Sometimes, however, in a paroxysm of acrocvanosis, gravity does not lessen, or lessens but slightly, the discoloration, which is thus shown to be spastic. Spastic blanching is sometimes seen: a pronounced and familiar form being the well known "dead finger." The alternations of areas of blanching, and of capillary and venous congestion giving rise to the "tatooed" appearance, and to the blue, white, and red stripes, disks, etc., are relatively infrequent. Sometimes the thermal and positional reactions indicate active capillary dilatation. more common than color changes in the hands are those in the nail beds, especially described in another paragraph.

In about one third of the cases, the skin of the trunk and extremities exhibits a number—sometimes a profusion—of vascular, pigmentary and troliferative anomalies—petechiæ, angiomata, tel-

angiectases, congeries of dilated capillaries or venules, or both, moles, yellow, brown, and black spots, papillary overgrowths. They vary much in number, in size, and in extent of distribution. I have observed the appearance of new stigmata of this kind, also the disappearance of old ones; and in several instances, spots appearing at first to be flat angiomata have lost their red color and become brown or black.

Both maculate and diffused pigmentation may be either transient or permanent. The occurrence of acanthosis nigricans, in connection with carcinoma of the intestine and other conditions in which irritation of the abdominal sympathetic or adrenal system is thought to exist, may be cited as an extreme instance of this tendency. In the cases under consideration the pigmentations vary in size from mere flecks or freckles to extensive areas, and in color from pale yellow to black. They may be localized or widely scattered, and may or may not be associated with cell proliferation. The ordinary brown or black "mole" is quite common, and is sometimes considerably elevated above the surface. In two cases, both in women, I have had an opportunity to observe pigmentation of two different types in course of development.

CASE XXIX.—Pigmented spots following a localized punctate eruption in a patient formerly exhibiting gastric criscs; eye signs, tricolored nails, thyreoid enlargement, palpitation. Miss A., aged seventeen years, of American birth and ancestry, on one side of Scotch, and on the other of German, extraction, tall, fair, brown haired and brown eyed, a college student, had complained of crises of nausea unassociated with vomiting, but attended with palpitation of the heart. They were not dependent upon food, but followed excitement or prolonged study. She had slight enlargement of the thyreoid gland, retraction of both lower eyelids upon fixation of the balls, and retraction of both upper lids in conversation. The nails were tricolored. No

organic lesion of any kind was discovered. The attacks subsided under treatment. Five years later, after graduation, she reported that she had remained well (except when crossing the sea), but consulted me in regard to a curious eruption upon the left wrist. It consisted of a number of red spots not raised above the surface, grouped in six areas, respectively of circular, oval, and irregular linear shape, the smallest about I cm. in diameter and the largest about 6 cm. in length and 2 cm. in width. There was no itching and no unpleasant sensation of any kind. The patient could not remember any blow or knock. In the course of six months some of these spots gradually faded, first to brown, and then to a yellowish brown, and at present one area remains of a faint pink hue, while the others show various shades of brown and yellow. The pink spot is still punctate, while the others are of a smooth, uniform tint.

CASE XXX.—Recent pigmentation around the finger joints and knuckles, lightened by gravity and pressure, in a patient presenting paroxysmal palpitation, thoracic pain dermography, eye signs and nail signs, without thyreoid enlargement. Miss E. C., aged twenty-three years, of American birth, German parentage, had a "nervous" mother, and seven brothers and sisters with "indigestion, biliousness, sick headache, nose bleeding, palpitation, and neuralgia.' The father was well. There was no history of tuberculo-The patient complained of palpitation sis in the family. of the heart upon any excitement, pleasurable or otherwise, accompanied with pain across the chest and frequently with hallucinations of sight and hearing. There was no disturbance of menstruation, and the thyreoid gland was not enlarged. The lungs were normal; the abdomen was negative; no enlargements, and no displacements of viscera could be made out. The heart beat was rapid, the first sound empty, the second sound sharp. There was a prominent Ludwig's angle. Pilomotor reflex was absent; dermography was marked; the hands were moist The lips were purple, the buccal and gingival and cold. mucous membrane was pallid, and there was a deep cyanotic gingival line on the lower jaw. The pharynx and palate were pallid and covered with congested vessels, dilated and tortuous veins being especially prominent. bubils were dilated and vacillating; the eyelids were tremulous when lightly closed; the upper lids were retracted upon fixation of the balls. The vessels of the fundus were dilated. There was a fine tremor of the hands. The skin

of the face and of the hands was oleaginous, but the silver probe did not produce a black mark. The nails were flat and tricolored (leaden, pink, and terminal red loop); the hands showed duskiness upon a yellow background, the duskiness running out upon elevation. Over the metacarpophalangeal and the first phalangeal joints was a dark yellow or brown discoloration, which lightened upon elevation and disappeared upon pressure. The patient stated that this was of very recent occurrence. The urine showed a trace of albumin, a few cylindroids, and a few red cells (not menstrual). The blood was practically normal.

The following instance is suggestive but less definite:

CASE XXXI.—Angioneurotic (?) adema of fect with purpuric cruption on leg, and ulceration at base of one toe; permanent (?) pigmentation at site of some purpuric spots; aerocyanosis, telangiectases, and pigmented spots; dermography; pilomotor reflex. C. W., aged sixty-three years, of Irish birth, a tailor, had had for the last twentyfive years attacks of pain in the feet, which he attributed to "rheumatism." He had also "spells" of shooting pain near the heart running into the left shoulder. There was a faint systolic murmur at the apex, heard also at the aortic cartilage, but not transmitted elsewhere. The lungs were normal. Over his body were scattered numerous telangiectases and pigmented areas, the latter circular in The hands were bluish, the color becoming intensified in cold weather. The face, cheeks, and nose exhibited many injected and tortuous vessels. The patient, however, was not an alcoholic and denied venereal his-Dermography and pilomotor reflex were present. The thyreoid gland was not enlarged. There was no eye The hands showed the usual changes when placed in and removed from cold and hot water. While he was in the hospital both feet suddenly became swollen and ten-der on the dorsum, without heat or redness. There was no fever. At the base of the right great too a suppurating ulcer with sharp edges developed. No sugar was found in the urine. A few days later purpuric spots appeared over the left leg extending posteriorly from the bend of the knee to the ankle. For the most part, they gradually faded away in the course of a few weeks. One or two, however, exhibited a tendency to become permanent pigmentations; but as the patient has disappeared from observation no definite statement is possible. The patient's father and one of his sisters died of hæmorrhagic phthisis.

Another pigmentary anomaly, less frequent than darkening, is leucoderma. There are but eight instances (and four of these in one family) among the present group of 200 cases. I believe it, nevertheless, to be fundamentally related to the condition of vasomotor ataxia. Minor degrees are apt to be overlooked; and also when it has occurred in child-hood and become so general that the patient simply seems to have an unusually fair skin, it is likely to escape recognition. Also will its occurrence in relatives or ancestors rarely be mentioned; it may easily be unknown.

Disturbances of physiological reactions are shown most markedly in regard to perspiration. Thus, there may be, among numerous other disturbances of this function, a tendency to profuse sweating from fright, excitement, or even slight exertion, in moderate weather, and sometimes in winter also. There may be, on the other hand, scantiness of perspiration, even in the heat of summer. Most of the patients will exhibit a tendency to excessive general discomfort in summer or in winter, accordingly as they belong to the ectatic or to the spastic type. These weather relations are often overlooked.

Among the transient, often recurrent, pathological conditions affecting the skin are urticaria, circumscript cedema, local and general, purpura, eczema, bullous cruptions, and various forms of crythema.

The test reactions of easy elicitation are those to emotion, to heat and cold, and to mechanical pressure. Concerning emotion, the patient will often complain of undue readiness to blush, or confess it if questioned; and it may be observed without special questioning in many cases. Also the patients will often relate instances of fright with pallor from slight and even ridiculous causes. Heat and cold are most readily applied by immersing the

hands or feet in hot or cold water, or by the use of compresses locally. The responses are, on the whole, similar in kind to those of normal individuals, but excessive in degree. Cold is more likely to produce cyanosis or blanching; heat to produce reddening; but heat may blanch and cold may red-There is, however, a difference in tints, easy to recognize but hard to describe. Stroking the red or blue skin sometimes blanches it, but to a more "dead" white, if cold has been applied. The Brown-Sequard reaction may be intensified or reversed. While a evanotic hand is reddening in ice water, its untreated, hanging fellow may become darker; but the color will usually run out, slowly, on elevation. Pressure is best applied by tracing upon the skin with a probe: blanching, reddening, or both (simultaneously or successively) may thus be elicited-ischæmic, hyperæmic, alternating, or mixed dermographism. Factitious urticaria is less common. In these patients severe bruises may result from slight and often unnoticed knocks. Cutis anserina is sometimes excited by exposure to the air, especially in a cold room; or by the brushing of the undershirt against the thorax, as it is removed. In other patients local pilomotor reflexes follow the track of a finger or a probe drawn across the skin. Drawing the fingers along the spine may excite a general gooseflesh reflex, usually less marked upon the lower extremities.

NAILS. In shape, the nails may be flat or curved; the surface may be smooth or ridged. They may exhibit changeable color or permanent zones of definite color. Usually they are blue, white, and red; the white area is the central portion, and pressure will increase its extent; while pressure (as with a ligature) applied to the finger proximally may change the color to a uniform red flush. The central area may

.

be simply lighter than the other zones, but not white. Nearly every case shows a deep red terminal linea loop of dilated capillaries. Sometimes the nails are uniformly leaden or pink in hue, except for this permanent deep red terminal line. The blue color may be confined to the root or extend over the entire nail, except the terminal free portion. In same patients, the free portion—i. e., the nail itself as distinguished from the nail bed—is intermittently yellow; and in the course of nail growth the change can be noticed in the central light portion as a somewhat sharp line. In a case of pseudoangina with paroxysmal tachycardia elsewhere reported and illustrated,18 the nails become black in cold weather, as in the classic Raynaud's syndrome. The whole nail bed may be involved, or only a segment, giving the banded appearance shown in the figure; which was reproduced for the artist's benefit by immersing the hands in ice water. This band may disappear in a few minutes or last half an hour or longer The area it occupies is ordinarily a dusky red. The discoloration may lighten when the hand is elevated, or may resist gravitational change.

The significance of these changes in the vascularity of the nail beds needs no pointing out. The importance of the cutaneous appearances, such as telangiectases and angiomata, as well as of the tendency to marbling of the skin, is that it shows imperfect, excessive, or at least aberrant, development of the vascular system in general. This receives a rather striking illustration in the two cases reported by Müller, in which part of the body exhibited marblelike discoloration, and part showed venous hyperæmia. In cold weather the markings became more distinct, while in warm weather they almost disappeared. This author ascribes the condition to

¹⁶ International Clinics, iii, Series 19, p. 53.

intrauterine segmental disturbance involving the metameres.

EYES. Many of these patients attract attention at once by some peculiarity of the eyes. Excluding now the pronounced exophthalmos which is seen, persistently or intermittently, in Graves's disease, the ocular appearances may briefly be summarized as follows:

Widening of the Commissure. This may be due to retraction of the upper lid, to retraction of the lower lid, or to retraction of both lids. It may be unilateral or bilateral; be permanent or intermittent, persistent or transient. It may be manifested spontaneously, especially in the excitement of conversation, or it may have to be elicited. In order to exclude the voluntary widening of the commissure within possible physiological limits and the voluntary dissociation of ball and lid movements (which is quite common among these patients), I have adopted the following method of procedure. The patient, holding the head level, is made to fix the eves upon an object held in the median line at about six or eight inches from the nose, which is then advanced toward the nose so as to produce excessive convergence. If this manœuvre does not cause retraction of the upper lids, the patient is told to elevate the eyebrows. The degree of exposure of sclera above the cornea determines whether or not the reaction is significant. I look upon this sign as a modification of Stellwag's.

Tremulousness of the Lids upon Light Closure. This is frequently found in Graves's disease, but also occurs in many persons who are not subjects of that disorder. So, too, von Graefe's sign, particularly that modification of it to which I have given the name of "hitch" (the interrupted descent) may be found, and yet the diagnosis of Graves's dis-

ease may not be justified by reason of the lack of

other necessary symptoms.

Dilatation of the Pupils. The pupils are most frequently dilated, usually bilaterally and equally. sometimes unilaterally or unequally. They respond to light and accommodation, but in some instances the contractility of the muscular fibres of the iris seems to be soon exhausted, and a vacillating pupil (almost a condition of hippus) is developed by repeated or prolonged testing. There may be alternations of contraction and relaxation during a continued stimulus of light. This is to be noticed especially in children, who cannot give a clear account of their symptoms or sensations. Such children may complain of headache, of indigestion, or, as they sometimes call it, "queer feelings" or "funny feelings," not very different from preepileptic auræ. These auræ sometimes precede headache; which may be fleeting, or persist for some hours, may be unilateral or general, and in either event may or may not be accompanied or followed by nausea and vomiting. Intermittent or persistent myosis is rare.

To exclude refractive errors and muscular anomalies as possible causes of the signs described, the tests should be made while the patient is wearing

corrective lenses.

Pigmentation around or beneath the lids, while

not very frequent, is yet not exceptional.

Pain in the eyes is not uncommon. It is not the ordinary pain of migraine and may or may not be attended with sick headache.

Drooping of Lids. I have seen but two instances of this—in mother and daughter. In Raynaud's disease there may be temporary narrowing of the commissure, contraction of the pupils, and ptosis; the exact opposite of the phenomena of Graves's disease and of the usual phenomena of vasomotor

ataxia. In Case XV of this series there is intermittent and partial ptosis of one eyelid associated with characteristic Graves's phenomena.

Distention of retinal vessels, both veins and arteries, occurs persistently or paroxysmally in many

cases.

Ischæmia of a spastic type is less common.

It is difficult to estimate the significance of the refractive errors, which nearly all these patients exhibit. They are usually astigmatic and hyperopic, less commonly myopic. The frequency of these errors in all sorts and conditions of men removes them from the category of diagnostic signs. In the subjects of vasomotor ataxia correction of the refraction and of the muscular anomalies that may coexist, greatly diminishes the frequency of paroxvsms, and sometimes entirely relieves certain symptoms, especially migraine, nausea, and gastroenteric crises. I am inclined, therefore, to put eyestrain high in the list of determining causes. Nevertheless, there are many cases in which such correction fails to alter the general course of the patient's life history.

THYREOID GLAND. This is usually, but not always, somewhat enlarged and soft. Sometimes the enlargement is intermittent. It is sometimes trifling, even in well developed cases of Graves's disease. It may be influenced markedly by position.

HEART AND VESSELS. The heart in most cases is easily disturbed. It is rarely irregular, unless there is an actual lesion. The first sound is usually short, often empty, reminding one of the fetal heart. The second sound, even in ectatic cases, is usually accentuated. This accentuation of the second sound may even correspond with low blood pressure. Patients exhibiting the permanent cyanosis of the extremities, or mottling of the skin, or in whom the

paroxysms are of the variety of passive congestion, usually have low blood pressure (from 90 to 100 or 110 systolic, and from 70 to 80 diastolic). exhibiting spastic phenomena may have permanently or paroxysmally high blood pressure, especially in constrictive migraine or pseudoangina, during the This may show itself less in the actual figures than in the reduction of the difference between the systolic and the diastolic pressures. Often, however, there is noticeable lack of correspondence between the brachial blood pressure and the apparent character of the other symptoms; as likewise between the condition of the external vessels and those of the deeper structures. Thus, flushing of the face may accompany a paroxysm of hemianopsia rationally attributable to temporary ischæmia or venous congestion affecting the visual centres, and there may be anginoid pain with low tension at the wrist. In the case with black nails, blood pressure was high during an attack, but quite low at other times. Pituitary infundibular extract will usually elevate blood pressure, but in one case caused depression. Tachycardia, or at least palpitation of the heart, is common. It is usually intermittent and paroxysmal, but when Graves's phenomena develop, it is often persistent. Murmurs are present in about ten per cent. of the cases, and actual valvular lesions in about one half of these. As cases progress, murmurs, muscular or orificial lesions, and changes in vessel walls that were not present in the beginning Throbbings and hæmorrhages have may develop. been spoken of in another connection.

MUSCULAR MOVEMENTS. Tremor in some portion of the body is not at all uncommon. Tremor of the eyelids has already been alluded to, and in some cases nystagmus is present also. Infrequently there is a twitching of the lids or perhaps of one lid—

upper or lower—which, as a rule, is intermittent. Tremor of the fingers is not rare. Sometimes there are paroxysms of general tremor, or frequent fits of shivering from a sudden cold draft or even without definite exciting cause. Trembling may be of emotional origin. It is in some instances controlled by the administration of parathyreoid substance; sometimes by calcium. Choreic movements are perhaps no more common than among the generality of persons. In the present list of 200 patients there are but four instances of chorea and two of habit spasm. In four cases there is note of nocturnal muscular spasm (extension of arms or legs, or both, not repeated) waking the patient; and sometimes preceded by a "pistol shot" sound. In one case, the muscular jerking may terminate a day time nap. In three cases there is frank epilepsy, two being petitmal. I have not counted the number of times in which epilepsy is mentioned in the family history, but it is more than six. All these may be coincidences.

FAMILY HISTORY. In almost every case in which the family history can be traced—for example, in 180 of the 200 cases studied for this paper—it is found to be rich in metabolic, nervous, and even distinctly angioneurotic disorders. As to the latter category, it must be granted to critics that the question of interpretation comes in. If the reference of the symptoms to angioneurotic disorder is incorrect in præsentia patientis, the like diagnosis of the similar conditions reported as occurring in "his sisters, his cousins, and his aunts" in absentia, is still more likely to be wrong. At all events, the family history is found to be rich in instances of disorders similar to those of which the patient complains, or of a related character. For example, one patient's crises are predominantly gastroenteric; the father is asthmatic; a brother and a paternal cousin suffer with hay fever; a paternal aunt has Graves's disease; a sister and a paternal cousin have "bilious spells." Again, a child exhibits angioneurotic œdema; the mother, migraine; the sisters, eczema, urticaria, menorrhagia; the grandmother, diabetes; an aunt has glaucoma.

Sometimes an angioneurotic history is traceable both on the father's and the mother's side; these patients exhibit the most varied symptomatology.

Tuberculosis is frequently found in the patient's immediate family or ancestry; less commonly in the patient himself. A rigorous statistical study would. of course, be necessary to determine positively whether this frequency in kin, or relative immunity in individuals, differs from that to be found among an equal number of persons taken at random; and the fact is not to be overlooked that a number of tuberculous patients exhibit some of the signs of irritation or of depression of the autonomic nervous system, particularly the dilated pupils, the afebrile flushings, and the hypotension of peripheral vessels; more rarely the tendency to retraction of the lids. I am inclined to believe that the connection between vasomotor ataxia and tuberculosis is fundamental. though I cannot here discuss its exact nature.20 The

¹⁰ So called "bilious" attacks, a rather vague term including many varieties of abdominal and cerebral disturbances, are not uncommon in the family histories or in the patients' own histories.

20 Allbutt (op. cit., p. 90) discusses the relationship between the "rheumaticogouty diathesis (which he had frequently found), eczema, and visceral neuroses." While rejecting any direct tie, he goes on to say: "Perhaps the discase most largely found in neurotic families beyond their neuroses is phthisis. In case after case I find phthisis in parents or kin. . . . For many years I have moted the frequent coincidence of phthisis and rheumatic fever in family trees, and I think this coincidence has been discovered by others. But what of the gout? Rheumatism and gout are certainly akin. . . A pure neurosis goes hand in hand with phthisis and acute rheumatism, but pains, which, like migraine, enteralgia, sciatica, etc., may in association be of a pure type, may in other instances be caused by the poison of gout, and these should be put in a separate class with the eczema and psoriasis of gout. In the

erethetic tuberculous type is recognized by many writers; but an apathetic type is no less common; and mixed cases are often seen. The patient with black banded nails is the son of a tuberculous father and a mother who has gastroenteric crises. He has himself recovered from pulmonary tuberculosis. In several cases reported in this series a similar association is mentioned; and it is noted thirty times in the 200 records. One other illustrative instance may be cited.

CASES XXXII and XXXIII.—Incomplete Graves's disease with migraine, acrocyanosis, and menorrhagia in the sister. Pulmonary tuberculosis and bleeding hæmorrhoids in the brother. Both exhibit nail signs, etc. Gouty and tuberculous parents. Miss P., aged eighteen years, a school girl, of American birth and Scotch and English ancestry, whose home was in a mountainous region of the south, suffered considerably at her menstrual periods, which lasted some seven or eight days, and were attended with great loss of blood. She was somewhat anæmic, and had migrainous attacks in the intervals between the menses. There was considerable enlargement of the thyreoid gland; some tendency to palpitation; cyanosis of the hands, tricolored nails, dermography, factitious urticaria; dilatation of the pupils, widening of the commissure, and a high de-

one class the neuralgias depend upon congenital defect of nutrition affecting the nervous apparatus itself. In the other class the nervous apparatus, originally healthy enough and even vigorous, is angered by a circulating poison. Yet, is there not some alliance beyond this? Is there not some remote pathological kinship unexplained by the humoral theory? Yes, I believe there is. I believe that further back there is some community of nature between the gouty and the neurotic habits, and to this we may ascend when we track out those phenomena which suggest that gout is itself originally a neurosis. Although there is then no gross alliance between neurosis, phthisis, and gout, yet one may trace the history of gout upward to a point of union with a divergent stock, which two, three, or four generations back had branched off into the tuberculoneurotic. In such cases, and I have notes of several of them, antigouty remedies are of no use whatever."

I have quoted this at some length, not because I accept it entirely, and although, not probably, the writer cited might himself now wish to modify the detail somewhat; but because, first, it records an observation closely paralleling my own; and, second, because it expresses fundamentally a profound truth which will again be recognized when in a few years hence the emancipation of pathology from the tyranny of a one eyed bacteriology—now happily progressing—shall be complete.

gree of myopic astigmatism with anisometropia. tion of the visual error relieved the migraine. The other symptoms disappeared under rest at the periods and medicinal hygienic treatment. Thyreoid enlargement subsided and the hands gradually assumed normal coloration. The patient is now thirty years of age and is practically well, except that when nervously excited the local cyanosis reappears and she feels "a lump in the throat," so that it may be necessary to open her collar. The father of this patient died at seventy-five of uræmia. The mother was highly neurotic, had gouty arthritis and gastralgic crises, and exhibited both eye signs and nail signs.

The brother exhibited the stigmata of vasomotor ataxia. but was not disturbed by any vascular symptomatology. About two years ago he was attacked with a cough and fever, and came to Philadelphia for examination. I found consolidation of the left apex, the sputum contained numerous tubercle bacilli, the patient had lost about twenty pounds in weight. He complained of painful, bleeding These were removed with the thermocauhæmorrhoids. tery; and appropriate treatment, hygienic, and medicinal, instituted for the pulmonary condition. He gained thirty pounds in weight, and the pulmonary lesions appeared to be quiescent. The signs of vasomotor instability, however, could still be made out. There was tuberculosis on the paternal side in several families and generations.

Gout²¹ is quite commonly associated with diabetes in the immediate family or in the ancestry, and when they occur dissociated, gout is the more frequent of the two; rheumatism—so called—and rheutoid arthritis are fairly common. Many cases exhibit a history of gout or so called rheumatism on one side and tuberculosis on the other. These patients rarely have evident tuberculous symptoms, but they frequently respond to the cutaneous tuberculin tests, even when they fail to respond to tuberculin otherwise applied. Whether or not this is to be brought into connection with the general sensitive-

²¹Herz (op. cit., p. 12) does not find the gouty tendency marked in many cases, nor does the occurrence of diabetes seem to him more frequent than coincidence will account for. He does, however, frequently find in the patient or in the patient's family, obesity or obdurate anemia, or both.

ness of the skin exhibited by most of these subjects would require a special and precise study to determine.

A tendency to cutaneous eruptions of various kinds, not always recognizable from the description, is marked. Of these, urticaria is by far the most common; but various forms of erythema, of purpura, and of eczema are also recognizable; and are sometimes observable in other members of the fam-

ily as well as in the patients themselves.

In this connection a significant series of phenomena is presented by two American born sisters, who suffer from gastroenteric crises, and both of whom were mistakenly thought to have appendicitis. One is an active business woman, while the other would be called by some physicians an "hysteric," although she works when able to do so. The father, a German, is said to be gouty and to suffer severely with eczema, but otherwise is well. I have never examined him. The mother, also German, is healthy.

CASE XXXIV.—Recurrent paronychitis; migraine; circumscript ædema; premenstrual epistaxis; transient pigmentation; transient hemianopsia; tricolored nails; dermography. The younger and more active sister presented a condition of chronic, recurrent vesiculopustular eruption around the nails, and a tendency to fissuring of the finger tips in cold weather. Occasionally she had sick headache. She was subject to hives, and frequently if she struck the hand or any part of the body—as by accidentally knocking against a chair or even by rapid removal of underclothing—a transient, colorless swelling would develop along the line of traction or pressure. The nose usually bled just before menstruation. She had attacks of transient, irregular, dark brown, "spotty" discoloration of the face, and with this, transient hemiopia and redness, swelling and burning of the feet and ankles. She had tricolored nails, dermography, factitious urticaria, and exaggerated pilomotor reflexes. She had no goître and no eye signs.

CASE XXXV.—Neurasthenia; varied visceral crises; chronic eczema; erythema exudativum with purpura; dermography; nail signs; eye signs. The weaker sister had

had several attacks termed "nervous prostration." She had undergone a shortening of the uterine ligaments, but still had many and diverse menstrual disturbances, varied with biliousness, sick headache, cardiac palpitation, syncope, mucous enteritis, and paroxysms of general tremulousness. There was a chronic eczema of the hands and sometimes a generalized moist eczema. I saw her in an attack of erythematous ædema of both legs, with purpuric spots on one thigh. She had also rheumatoid arthfitis, and presented typical nails, dermography, and the eye signs. The thyreoid gland was not enlarged. The urine contained albumin intermittently, occasionally blood cells, cylindroids, urates, and oxalates.

Previous History of the Patient. The pathogenic tendencies of the patient become quite evident when a sufficiently careful anamnesis is made. They begin to be manifest, as a rule, in childhood, and it is concerning children, therefore, that mistakes in diagnosis are most likely, from want of previous manifestations. Here the family history and the personal characteristics are valuable. Recognition of the child's tendencies is of importance not only for the immediate attack, but also that a regimen may be instituted which will correct them and prevent life long recurrences of the varied syndromes. The individual presents in reduction what the family presents in large. His first symptom may have been colic, migraine, epistaxis, or hives. His present symptoms may be hives, migraine, epistaxis, or colic. Intermediately he may have had paroxysms of diarrhœa, polyuria, asthma, hay fever, palpitation of the heart, glycosuria, hæmoptysis. Nor does this exhaust the beginning, middle, or final list. Care is obviously necessary in making the record to exclude the common symptoms of adequate causation —the boy's attack of nose bleeding from contact with his comrade's fist; or of colic, purging, and vomiting following a surreptitious visit to a neighbor's orchard or the candy shop. In a serious investigation, however, such care may be taken for

granted.

It is somewhat difficult to estimate the importance of the history, given by adults, of eruptive fevers in childhood; especially when "third" and "fourth" attacks are spoken of. I have seen, both in children and in adults, angioneurotic storms mistaken for measles, roseola, or scarlet fever. I have myself made the mistake of quarantining for scarlet fever a boy whose family history, previous personal history, and physical characteristics would nowadays put me on guard. The attack was one of erythema, with repeated desquamation. In a case observed at Jefferson Hospital, erythema and angioneurotic ædema developed while the patient was being exhibited to the class at a clinical lecture, and the parents volunteered the statement that the appearance was the same as what they had supposed, in a previous attack, to be scarlet fever. In the case of a boy seen at the Polyclinic Hospital, on removing the clothing for examination there appeared first a general crythema, soon replaced by rude geometrical designs in red, white, and blue lines and patches. This is the patient I have referred to elsewhere as the "tatooed boy." In the case of pseudoangina previously cited, similar exposure produced red and white circular patches. I have seen many curious forms of transient rashes-red; red and white; red, white, and blue; red and blue; but never blue and white.

The scarlatiniform and rubelloid attacks are frequently accompanied with nausea, vomiting, abdominal pain, sometimes albuminuria, not rarely fever; and are probably of toxic excitation. As isolated occurrences, adequately caused, they would be of no importance other than that derived from their ætiology. When inadequately caused, or forming part

of a series of varied vasomotor disturbances in an individual or family, they acquire new significance.

I have elsewhere²² recorded an instance of excessive susceptibility to quinine, twice manifested by transient scarlatiniform rash, fever, ædema, and delirium, in a boy who, as an infant, had had scarlatina sine exanthema,²³ announced by anuria and general anasarca. This boy is one of a family exhibiting marked vasomotor disorders.

A paternal great uncle suffered from pulmonary hæmorrhages for many years, dying in old age of acute pneumonia. (Whether he had tuberculosis I cannot say; the family said not.) This uncle's daughter is Case III of my first series (transient hemiopia, repeated erythema, etc.), and has now apparently recovered from the tendency to angioneurotic crises. The boy's father and a paternal aunt and her son have hay fever. Another paternal aunt has had repeated retinal hæmorrhages; another had as a child repeated spells of profuse spontaneous epistaxis, which ushered in a protracted case of chorea, and ceased with the latter. A brother, who as a young lad was subject to spontaneous epistaxis and marked ecchymosis or circumscript ædema from slight knocks, has apparently outgrown these symptoms, but now has hay fever. A cousin of his father's for many years had asthma whenever he stayed in the country—even for two or three days—in summer time, and died of angina pectoris. A paternal uncle died of diabetes, and the son of this uncle has hay fever. Another paternal cousin had a prolonged illness with varied symptoms of autonomic nerve disorder, that was diagnosticated by a well known neurologist as exophthalmic goitre, by a distinguished internist as Addison's disease, and by me as vasomotor ataxia. The lady recovered perfectly; tachy-

²²Transactions of the Association of American Physicians, xvii, 1902. This paper contains a more extended discussion of the general subject.

²⁸There is no question of diagnosis; it is my own, confirmed by an expert of international repute. The boy's brother, aged three years, had frank and severe scarlatina. The infant was kept under close observation; he had slight elevation of temperature without angina or rash (unless it appeared and disappeared during his night sleep) for three days. Dropsy and anuria developed suddenly on the fourth day. He was then placed in the same room with his brother; recovered under treatment; and had an uneventful convalescence, followed by otitis media. There was no desquamation.

cardia ceased; glycosuria and pigmentation disappeared; and the thyreoid, never very large, returned to normal size. Another paternal cousin was subject to syncope, with cyanosis of the lips; now, to cyanosis without syncope. Distinguished clinicians examined her repeatedly and found no cardiac disease or defect or other organic lesion. Two paternal uncles, the father and the paternal grandmother have leucoderma; a fourth paternal uncle is subject in winter to blue hands, with deep fissuring of the finger tips.

The following case illustrates the connection of scarlatiniform erythema with angioneurotic visceral crises and the Graves's syndrome, as well as the liability of good observers to make mistakes in diagnosis.

CASE XXXVI.—Erythema exudativum following acute gout (?) in a subject of chronic Graves's disease, subject to gastrointestinal crises. Just before leaving Philadelphia for this meeting I saw in consultation a woman, aged sixty years, who, following an attack apparently of acute podagra, was attacked with a scarlatiniform rash beginning on the face and spreading over the entire body. With this occurred suppression of urine, and on resumption of the secretion under the influence of diuretics it was found to contain considerable quantities of albumin, but no blood and no casts. There was no sore throat and none of the characteristic signs upon the mucous membrane which are common in scarlatina. The patient was confident that as a child she had not had scarlet fever. Of two former consultants one, a dermatologist, had inclined to the diagnosis of scarlet fever; the other, our foremost local authority upon the eruptive fevers, had negatived this view.

Flaky desquamation occurred within three days—before the rash had entirely disappeared, but while it was fading; and in the course of two or three days more, desquamation continuing, the skin remained but slightly congested here and there. With no apparent reason, temperature suddenly became elevated, a dusky uniform rash reappeared upon the face, and in the course of twenty-four hours had spread over the trunk and arms. Albumin, which had disappeared, reappeared. A few purpuric spots had been noticed upon the thighs prior to the eruption. These had disappeared. When I saw the patient the recurrent rash was of about thirty-six hours' duration and had now spread to the knees. During the height of the fever the patient had had hallucinations of various kinds. The pulse had been

120. When I saw her the mind was clear, the pulse rapid, but of low tension. What attracted my attention at once was marked exophthalmos, which upon inquiry was said to have been existent for many years. Von Graefe's and Stellwag's signs were present. The pupils were dilated, but the reflexes normal. A probe drawn over the skin left a white mark where the skin was blanched beneath it. Pressure with a broad blunt surface, like the thumb, produced but a momentary whitening which quickly disappeared. There was, however, marked ædema over the entire surface occupied by the rash. The urine was secreting freely and was free from albumin. When the recumbent patient drew up her legs in bed the color slowly faded in the elevated portions of the thigh; but returned when the knees were again lowered. Application of ice was followed by blanching and pitting, which persisted for three or four minutes. Application of hot water caused increase of red-The nails were a very pale purple (mauve), with a deep red line at the terminal portion. Elevation of the hand and arm failed to bring about any gravitational change in color. The veins were not markedly distended. Petechiæ or telangiectases, if existent, were masked by the rash; at all events, none were discovered. This patient is subject to gastric crises, with and without headache, to abdominal cramps, and serous diarrhœa. no evidence of organic visceral lesion.

A history of neuralgic pains in various parts of the body is common. Some patients complain frequently, others only occasionally in the course of years. The "neuralgias" may alternate with, displace, or be displaced by the splanchnalgias. Leg cramp is frequent and not rarely rises to intermittent claudication. It is in many cases associated with a tendency to painful erythema of the feet, which might justly be termed erythromelalgia, and is sometimes miscalled "gout" or "rheumatism" or "ervsipelas." Intercostal or, at least, thoracic pain is a not infrequent symptom. It was particularly marked in the case of a man, aged thirty-two years (Case XXXVII), in which percussion was impossible during the attack on account of the exquisite tenderness to the slightest jarring.

The significant signs in this case were the paroxysmal recurrence of the pain, which was either præcordial, submanubrial, or subxiphoid, and its association with cough and either bloody expectoration or a sense of choking relieved by the vomiting of mucus, which was occasionally blood streaked. The eyes showed the characteristic signs. The thyreoid was slightly enlarged. Pilomotor reflex and dermographism were present. The skin was moist, the hands cyanotic, the heart rapid, with invisible apex beat and accentuated aortic sound. This patient used both to-bacco and alcohol to excess, facts which nevertheless account for but a portion of the symptomatology. The lungs and larynx were apparently normal.

As previously pointed out, paroxysmal pain may affect especially the præcordium and the arm; sometimes the attacks so closely resemble angina pectoris as to excite the gravest concern. The substernal location of pain, however, is not so frequent as the præcordial. Among others, the patient with black banded nails exhibited symptoms of this type. It may be, as certain distinguished observers hold, that "pseudoangina is a pseudodiagnosis"; and it is true that indubitable angina pectoris is the terminal event in some of these cases. Yet unless the progress of science should bring proof to the contrary, I shall continue to believe that in the beginning, in such cases as I have in mind, the paroxysms are of the same order as the angiospastic manifestations occurring elsewhere, and that only late in their progress do aortic or coronary lesions arise as a result of the repeated disturbance of neurovascular function and nutrition—whether it be vasovagal or less sharply located.

That the so called neuralgic pain occurring elsewhere than in the præcordium is, like intermittent claudication, angiospastic in character, is well illustrated by the following intermediate.

trated by the following instances:

Case XXXVIII.—Angiospastic "facial neuralgia" in a patient recovered from exophthalmic goître; cardiomyopathy; visible distention of temporal artery; relief by ni-

trites; history of anginoid attacks previously; dermography; nail signs; cutaneovascular signs; pigmentations; interesting family history. Mr. L., of American birth, German parentage, aged sixty years, had exhibited the characteristic phenomena of Graves's disease some fourteen years ago, when he was under the care of a competent physician in a distant city, and recovered from the obvious symptoms in about eight months. At that time he was an otficer of police. His present complaint was of heart consciousness, with occasional palpitation and dyspnœa upon exertion, and of a peculiar "neuralgic" pain in the right temporal and maxillary regions. In 1891, five years before the goitre and exophthalmos were noticed, he began to have attacks of sudden præcordial pain, sometimes extending down the left arm, and later accompanied with a feeling of suffocation and faintness. They would last with varying severity for some minutes. The attacks were at first infrequent, but the intervals gradually became shorter and the symptoms more severe. Nevertheless, he increased in weight from 180 to 237 pounds. Finally, the dyspnæa became almost constant, except when the patient was lying With this would be associated, especially on arising in the morning, dizziness, faintness, and dimness of vision. At times there was buzzing in the ears. cardia, goitre, and bulging of the eyes now developed. Rest was advised, menthol administered, and the symptoms gradually faded away. At the same time the patient lost flesh, so that at present, and for many years he has weighed under 160 pounds, although he is six feet tall. His hair is black, his eyes bright, his skin in general somewhat flushed, and his general appearance much younger than his years.

About two years ago he began to experience his present symptoms, which increased in severity. The pain in the head was sudden, sharp, and stinging. It lasted less than two minutes; during which time he could not speak and usually bent forward, propping the head on the hand and the elbow on a table or chair arm. The pain usually began in the right temple and radiated toward the angle of the mouth and the angle of the jaw; but occasionally the At first it might recur several times order was reversed. Recently there had been no daily, or not for several days. long interval, and any motion of the jaw, as in talking or eating, after a period of nonuse, might precipitate the pain. The teeth were good, and the alveoli not tender to pressure. In the attack the face was pallid and the temporal

artery of the right side (which ordinarily was tortuous but not distended, and was comparatively soft) enlarged visibly and became harder. The right temple, cheek, and jaw were tender. This tenderness subsided a few minutes after the sharp pain disappeared.

The pulse was irregular and intermittent. The rate varied from 80 to 100, becoming more frequent and more irregular on exertion. The radial arteries were somewhat hardened, but small and compressible. Systolic blood pressure was 95, diastolic 70. Cardiac dulness was increased longitudinally and transversely. There was no defined apex beat, the impulse being diffuse and wavy. The cardiac sounds were short and feeble, lacking both muscular and valvular tone. There was no murmur. The tracings indicate myocardial degeneration. No pulsation was seen in the neck, but there was visible epigastric pulsation. The liver was enlarged, but not tender. The spleen and the kidneys were not palpable. There was no ædema. The thyreoid gland was hard, deeply seated, and slightly enlarged bilaterally. The eyeballs were still slightly prominent, the sclera being exposed both above and below the cornea. No additional retraction of lids, either spontaneous or provoked, was made out. The lids showed no tremor. The forehead could not be wrinkled by elevation of the eyebrows. The pupils were round, equal, and promptly and rapidly react to light and accommodation. The eye grounds were redder than normal. There was hyperæmia of the optic disk, and the veins were somewhat The lungs were normal, the tonsils were large, the pharynx injected, the nose and larynx normal. Tentative administration of a minute dose of nitroglycerin (I minim of a 1 to 500 solution) at the inception of the attack of pain diminished its intensity and reduced the duration of the tenderness. The continuous administration of nitroglycerin, together with rest, regulation of diet, and the use of a good tincture of cactus, has improved the cardiac action and seems to have brought about disappearance of the facial pain. This patient exhibited sluggish dermographic blanching and reddening. The nails were curved and tricolored. The skin was covered with numerous angiomata, tclangiectases, and varicosities. There were many pigmented spots, and on the legs, marks of old, healed varicose ulcers.

The patient had had the usual diseases of childhood, and at twenty-two years of age a second attack of diphtheria. When nineteen years old he had a sudden, violent nasal

hamorrhage without known cause, losing nearly a pint of blood. There was no venereal history. He had used to-bacco, coffee, and alcohol in moderation, but not since 1896. There had been no indigestion, the bowels were regular. The urine showed occasionally a trace of albumin and a few epithelial cells and leucocytes; otherwise it was nor-

mal. The blood was normal.

His father died at sixty-seven, of diabetes; his mother at seventy, of "heart disease"; one sister, at twenty, of "consumption"; one brother, in infancy, of "meningitis." He had had ten children, of whom five were living. One of these had hay fever; one was "nervous"; one had a tendency to bleed freely from slight cuts and to apparently spontaneous nasal bleeding. Of the five dead, one had had "consumption" and one "heart disease"; three died in infancy of infectious fevers.

Causation as an Element in Diagnosis. symptoms of vasomotor ataxia in general may depend upon relatively sluggish, or relatively excessive, response to extrinsic or intrinsic stimulus, inhibiting or excitatory. They are caricatures or exaggerations of phenomena observable in normal individuals upon adequate causation, and their occurrence without traceable cause, or with relatively slight cause, is a diagnostic factor of considerable import. So, also, is their tendency to follow meteorologic changes, fatigue, or emotion. By emotion is to be understood long continued anxiety or other form of psychic strain, as well as sudden excitement. Several illustrations of the former sort have been given without particularizing. Among them have been money worries, family quarrels, waywardness of children and others, grief over deaths, a broken engagement, a secret marriage. Among the latter are fear, fright, sorrow, sometimes anger-but, although less frequently, pleasure also. Three additional instances, two of acute, the other of gradual development, may be cited.

Case XXXIX.—R. D., whose symptoms quickly followed the loss of two children, complained of "sticking sensa-

tions" from the larynx downward to the abdomen, difficulty in swallowing, belching of gas, and vertigo, with cardiac palpitation on exertion. The thyrcoid gland was slightly enlarged, soft, elastic. There were no eye signs. The heart sounds were empty: faint murmurs were heard in the veins. There was no thrill or murmur in the thyreoid. At night the patient complained of noises in the ears. The conjunctivæ were much injected. The urine showed a faint trace of albumin. Dermography, factitious

urticaria, and tricolored nails were observed.

CASE XL.—Miss C., a painter, aged thirty years, had been going through a prolonged period of severe mental strain and sorrow. She had been laid up for four weeks with an attack termed pleurisy, the symptoms being chills, fever, pain in the back, and pain along the border of the ribs. Since then there had been a constant cough, short, hacking, and without expectoration, which became worse upon emotion. It was frequently accompanied with chill, which would last for a few minutes and then give way to general tremor. No fever followed. Previous to this she had from time to time experienced what she described as a "surging feeling" in the head, with a sense of tension in the eyes; but there was no neuralgic pain, no visual disturbance, and no vertigo, either then or at any other time. There was headache only the day before the menses. What brought the patient to my office was the suspicion of "heart disease," caused by pain in the præcordium, intermittent and sharp. She frequently felt faint with the attack, but did not lose consciousness. No lung lesion was discoverable. The mucous membrane of the larynx was red and slightly swollen, the congestion disappearing under the application of suprarenalin. The heart was rapid under the excitement of examination, but the patient stated that this was not its usual behavior. The first sound was short but normal in character, the second sound was not sharpened; the vascular tension was low, the hands cold, the nails tricolored. The blood showed slight quantitative anæmia; malarial organisms were not found. The thyreoid gland was slightly enlarged. The eye signs were present. The "pleurisy" in this instance was probably the localizing determinant.

CASE XLI.—Mrs. R. M., aged thirty-eight years, complained of pain running around the lower periphery of the left breast and then down the left arm. The attacks came on after fright or any sudden emotion. The pain might last all day or sometimes only an hour. Sometimes there

was sudden stabbing pain, and she lost power in the arms and objects fell from her grasp. Once she had an eruption on the breast, but did not know its character. A baby with the mother showed Hutchinson's teeth. During the paroxysm of pain in the chest the hand "turned black" on the palmar side of the fingers; patches the size of a pea appeared. Sometimes the whole hand and fingers might be covered with "white patches," and the hands turned cold. Distended capillaries were evident over the chest, the nails of the left hand were dusky, and were said to become black during the paroxysms. The thyreoid was slightly enlarged. No heart or lung lesion was demonstrable. "White" dermographism was found. Factitious urticaria could not be developed. The eye signs were indefinite.

SURGICAL EXPLORATION.

I have already referred to the fact that surgical exploration or even operation may be undertaken under a mistaken diagnosis of the character of the visceral crisis; or deliberately to settle the question; or even as the only possible curative procedure. It it fully justified. Though the patient may be angioneurotic, he may have appendicitis, cholecystitis, calculus or ulcer; and better operate unnecessarily in a case of ædema than neglect to operate in an inflammatory case. In laryngotracheal cases, prophylactic tracheotomy may be needed. I have mentioned the tabetic who died suffocated; and Rudolph's and Morris's cases are likewise in point. Moreover, the results of delayed circulation, of hæmorrhage, and other events involved in, or following upon, a visceral crisis of the character discussed, may be such as only surgical measures can properly deal with. This is well illustrated by cases which Osler cites. The following instances have come under my own observation:

CASE XLII.—Pseudoappendicitis. Miss M., aged twenty-two years, sister of the younger patient who died in hemplegic coma (Case XXVIII), suffered with severe abdominal crises, whose frequent relation to the menstrual period had led to the diagnosis of ovarian neuralgia. The

only attack in which I saw her occurred in the menstrual interval, and was accompanied with nausea, vomiting, rigidity of the abdomen, and exquisite tenderness over Mc-Burney's point. There was but slight elevation of temperature. I thought it wise to call a surgical colleague, and we both decided that, despite the possibility of error in diagnosis, the line of safety lay in opening the abdomen. The situation was explained to the patient and her family. An appendix apparently normal was found and removed. It had been pressed upon by a much congested ovary which was not disturbed. Since then there has been no return of the pain. The patient has had several attacks of hemianopsia and retinal hæmorrhage. There is occasional albuminuria.

CASE XLIII.—Pseudoappendicitis. M. X., aged nine years, was the child of a father presenting marked symptoms of vasomotor ataxia, a condition shared by many members of his family. Two of her cousins of nearly equal age had suffered like herself with severe and frequently recurrent abdominal crises. In one of these children, living in New York, the attacks had ceased after a course of diet and atropine advised by Dr. A. Jacobi. The other, living in another city, had been operated upon and a minute fæcal concretion found in the appendix. In my patient, hygienic and medicinal treatment continued over some years, had increased the interval between attacks, but had failed to prevent them; and the nutrition of the child was evidently failing. A surgical consultant agreed that it would be wise to open the abdomen. An appendix macroscopically normal was removed. A pathologist reported that the mucous membrane was thinned and might eventually have become perforated. The effect of the operation was good. The abdominal crises disappeared and the patient took on flesh and strength.

I also remember distinctly the case of a man who in the early '90s was operated upon by a distinguished hospital colleague with my concurrence; to our great chagrin, no lesion of the appendix was found. The patient, however, was well satisfied, as distressing colic of long duration was completely relieved. This was before I had learned to look for the stigmata of vasomotor ataxia in such cases, and the notes are silent in this connection.

CASE XLIV.—Hepatic crisis; operation; no lesion. Miss F., aged thirty-six years, a relative of S. M. (Case XLVI), and a typical subject of vasomotor ataxia, had been operated upon for appendicitis in a distant city. I do not know the details of the symptomatology, or the lesion found, if When I saw her she was slightly jaundiced and gave a history of having had, for two or three years, attacks of hepatic colic. I was unable to satisfy myself either of the presence or of the absence of gallstones. geon called in consultation thought he detected decided tenderness over the gallbladder, and it was certain that the patient winced under the manipulations, of the object of which she could not have been ignorant. She was not. however, hypochondriacal or hysterical. There lacked any recent history of gastric or duodenal catarrh, although among the other symptoms of vascular disorder in the patient's history were gastric crises. Under the circumstances, explaining to the patient that the procedure was exploratory and not without hope of improvement from the operation itself should we fail to find a calculus, incision was made and nothing abnormal discovered. Here, too, the result was good. I have seen the patient recently, and in the six years that have elapsed since the operation she has had no disturbance of any kind and has put on some twenty pounds of flesh.

It is almost certain that in these cases there is a disturbance of local circulation, and it is probable that with the change made mechanically by the operation—perhaps in the development of anastomotic vessels, perhaps in some molecular shaking of the cells which breaks up their morbid habit—the determining cause of the disturbance disappears. In the following cases the nature of the lesion was very clear, and the symptoms not sufficiently urgent to suggest operation.

CASE XLV.—Pseudoappendicitis in a case presenting circumscript & dema, thyreoid enlargement, eye signs, and cardiac derangement. A. G., aged thirteen years, school boy, of Russian parentage, Hebrew race, was subject to attacks of angioneurotic & dema occupying the back of the hand and the upper lip. There was a history of general anasarca accompanied with reddening of the skin (according to the parents, scarlet fever) two years previously. The swellings

came suddenly, lasted fifteen to twenty minutes, and passed away suddenly. The thyreoid gland was slightly enlarged. Eye signs, nail signs, dermography, and factitious urticaria were present. The heart was irregular under excitement, but regular when quiet; the first sound was short and sharp; the second aortic sound was sharpened; rate 78. The pulse was small and of moderate tension when the patient was quiet. The lungs were normal. Hæmoglobin was 85 per cent., red blood cells proportional. On one visit this patient reported that following an attack of ædema of the left half of the lower lip and of the back of the left hand, which had apparently been brought on by cold bathing, "blisters" appeared on various parts of the body, which lasted a few hours and then disappeared, after which he was seized with severe abdominal cramps and vomiting. There was rigidity in the right iliac fossa, and tenderness on pressure, not exactly at McBurney's point, but in that neighborhood. There was no fever and no leucocytosis. The patient was put at rest and food withheld for about thirty-six hours, when all symptoms disappeared.

CASE XLVI.—Pseudoappendicitis. S. M., aged eleven years, school boy, was one of a highly neurotic family. His uncles were typical subjects of vasomotor ataxia. His mother exhibited eye signs and nail signs, was subject to "bilious spells," and was unable to take quinine, as it produced a "bright red rash with itching." The child was easily upset by improper food, and was subject to fits of trembling upon being startled, when excited over his lessons, and sometimes without discoverable cause. In the fit his heart thumped, he felt cold, and became pallid, sometimes sweating profusely. He was bright, intelligent, and active, and not desirous of shirking school. He had pink nails with deep terminal red line; the skin was mottled; dermography and factitious urticaria were readily pro-Eye signs were not well marked; the heart was normal; the thyreoid gland was not enlarged. four times a year, without discoverable indiscretion in diet, he had violent colic and high fever, with intense pain in the appendix region, but without vomiting or purging, and usually, but not invariably, without rigidity or tenderness. Sometimes there was general flushing of the skin, sometimes a localized erythema, sometimes no cutaneous change. The paroxysms recurred several times daily over a period of three or four days, if untreated. They might be cut short, however, by withholding food; counterirritating, or applying heat, over the right iliac fossa; and administering

magnesium sulphate in small, frequent doses with a minute dose of morphine. The resulting stool was watery, and did not show mucus or blood, or evidence of irritating food. The boy could not take even a minute dose of atropine, but apparently is improving under thermic measures (hot and cold douching to the spine, etc.).

The susceptibility to drugs (so called "idiosyncrasies") exhibited by this boy and his mother is shared by many of these patients. Elsewhere I have given a number of instances.

In concluding the citation of cases it may be well to repeat that some of the personal characteristics, pathological events, and family relationships here described, may be found in persons who do not exhibit angioneurotic disturbances; and that it is not any single sign, but the association of a sufficient and significant number of them, with the symptoms and the pathogenic tendencies in individual and family history to which attention has been called, that is of diagnostic import.

I am aware that this paper and my former communications on the same general subject are open to two criticisms: 1, That the condition suggested

²⁴In my previous communication to this association (*Transactions of the Association of American Physicians*, 1902, p. 645, et seq), I have discussed this phase more at length and suggested certain evolutionary considerations. There is an excessive vasomotor lability associated with the "artistic temperament," and accordingly many of its signs and some of its pathological results are frequent among actors, musicians, novelists, painters, poets, orators. Also in some men and women of high intellectual capacity in other fields (science, jurisprudence, statecraft, commerce, finance, etc.), its stigmata, but less frequently, its more severe morbid consequences, will be found. If I should say that upon free and full cerebral circulation depends the capacity for sustained mental work or sudden coup—that this necessitates a labile vasomotor apparatus—and that according as inhibition, regulation, compensation (*i. e., taxis*) are adequate or inadequate, the quality and quantity of intellectual output will be influenced—doubtless the charge of "hypothesis" and "speculation" would be well founded. It is a guess, true—but it may be a good guess. An adequate study of this far reaching subject will demand a more accurate discrimination among patients, and the kind and severity of the symptoms to which different classes of men and women are specially liable, than I have so far attempted.

as a basic factor in the pathogenic synthesis is hypothetical; 2, that even granting the reality of this basic condition of vasomotor ataxia, its scope has been unduly extended by attempting to drag into its meshes a variety of phenomena which medical science seeks to differentiate rather than to con-

glomerate.

To the first of these objections the reply has been made that in the very nature of things, anatomical demonstration is not only difficult, but necessarily inconclusive; that animal experimentation can here help us only as it enlarges general physiologic knowledge; and that the designation applied to these conditions describes in the most general phrase possible the fundamental element in their physiological pathology. The patients do not ordinarily die of the early attacks, and when in later years they succumb to angina, apoplexy, uræmia, pulmonary œdema, and like terminal events, the lesions found at necropsy represent the results of long continued disturbance, and neither the cause nor the mechanism—nor even the fundamental anatomical expression—of its functional beginnings.

Even the fortuitous surgical demonstrations already spoken of exhibit merely the correspondence between cutaneous and visceral phenomena; they do not help us as to the basic facts; and in some instances the findings, although explanatory of certain symptoms, represent the results of long continued neurovascular disturbance, not its beginnings. What lies behind the failure in vasomotor taxis is yet to be determined. Neither physiology nor pathology, neither morphology nor chemistry, has yet given us the data for a definite solution. Here, while refraining from hypothesis, I may mention Wiesel's suggestive researches on the distribution of chromaffin; and the work of Uhlenlut, Sachs

Seber, and others on the chemical differences in the blood of different species of animals and even of different races of men, as exhibited by serodiagnostic methods.²⁵ The occurrence of autohæmolytic phenomena, most markedly in paroxysmal hæmoglobinuria, but in less degree in all the varieties of vasomotor ataxia, must be of deep significance.

The second objection entirely misses the point of these communications. Graves, Basedow, Raynaud, Weir Mitchell, Quincke, Schönlein, Henoch, Allbutt, and others have, so far as it has been possible, delimited and discriminated. Had they succeeded in giving definite and exclusive outline to the various pictures, these would still constitute but segments of a circle having a common centre. But examination shows no such sharp lines; we deal instead with the irregular curves of the pieces of a "puzzle picture"—and not a puzzle in which hollow here, meets and fits projection there, but, on the contrary, one in which there is much and repeated overlapping. Only when the overlapping portions are correctly adjusted, can the different pieces fall into place and the general design become evident.

The very nomenclature is significant. In so far as special associations of phenomena which more or less frequently occur or recur together have received identifying clinical designations, such designations are either a, the names of symptoms or of symptom groups, or b, the names of individuals who have called attention to such symptoms or symptom groups. In no case is there an accepted title based upon fundamental morbid anatomy, precise pathological chemistry, or definite and exclusive actiology. The terms hemicrania or migraine, hay fever or idiosyncratic corvza, local syncope, acro-

²⁵Max Seber, Moderne Blutforschung und Abstammungslehre, Frankfurt am Main, 1909.

paresthesia, acrocyanosis, drug idiosyncrasy, purpura, hæmophilia, circumscript œdema, erythema, urticaria, asthma, erythromelalgia, symmetrical gangrene, paroxysmal hæmoglobinuria, gastralgia, enteralgia, etc., are, at best, apt descriptions—which leave us no less ignorant of causes and underlying processes when taken from the Greek, than when

they are expressed in the vernacular.

Nor do we find any of these symptoms or syndromes standing sharply defined and alone. In almost every instance—certainly in the life history of patients and families followed and traced with sufficient care over a period of years—they will be found in considerable number and in changing association. When the same individual presents today one of these related syndromes, next year another, and five years hence a third; when such superficially opposite syndromes as Graves's and Raynaud's are observed at the same time in the same patient, perhaps in association with tuberculosis, or in a member of a tuberculous family (instances of which coincidence others, as well as I, have placed on record); and when critical analysis of the literature discloses under each syndrome name, many cases which might almost as well have been placed under any one of half a dozen other designations (the mere accident of the time of observation by the reporting physician apparently determining its classification)—the conviction is inescapable that underlying them all is a fundamental imperfection, which, under the incidence or coincidence of different ex-

²⁶In this condition, of course, as in some others, there is something more than mere disorderly vascular action. In a case now under observation the patient's serum is continuously hæmolytic to his own corpuscles in the test tube, but hæmoglobinuria occurs only in crises provoked and provocable by cold, and the patient while not manifesting Raynaud phenomena has the ocular and cutaneous stigmata of vasomotor ataxia. A detailed report will be given hereafter.

citants and determinants is manifested in a variety of results. It is for this unity amid diversity that I have sought; and, following the example of the Cuvier school of naturalists, for such external and easily recognized characteristics as might identify with reasonable assurance the class of persons in question.

During the many years that I have been able to follow a number of these patients, the recognition of their constitutional liability has been helpful both in the understanding and in the management of their disorders. To know it, not only prevents one from mistaking disorder for lesion, but also renders it unnecessary to resort to an ever new "Mesopotamia" for comfort, as from time to time the kaleidoscope is turned. Indeed, a single designation of this "blessed" order would often fail to cover the phenomena of a single paroxysm; and to fit with such cloaks the phenomena presented by some patients in the course of a few years, might empty the wardrobe of scriptural geography. Moreover, the symptomatology of intercurrent ailments is often profoundly modified by the constitutional tendency of these persons to vasomotor-trophic disorder; and both diagnosis and treatment may go astray when such liability is unknown or overlooked.

Many of these patients have at one time or another been termed by some physician, "neurasthenical," "hysterical" or "hypochondriacal"—perhaps all three. That neurasthenia, hysteria, and hypochondriasis are legitimate diagnoses in many cases may be granted, but in the class of persons whom I have in mind they fail to cover the field. Concerning the relations of vasomotor ataxia with neurasthenia, with hysteria, and with hypochondriasis, much could be said and more is still to be learned;

but upon this phase of subject I do not now desire to enter.

I have hitherto spoken of the visceral and other manifestations of vasomotor ataxia as if they were dependent solely upon vascular aberrations. however, has added to this conception something which, while implied, was not explicitly expressed in my first communication, nor was it so definitely conceived by me as he has described it. Basing himself largely upon the researches of Rosenbach, he observes that there is normally an active increase and diminution (diastole and systole) in the calibre of the interstitial lymph spaces, with pressure changes in consequence; and that from even a slight disturbance of this mechanism, widespread functional and trophic disorder can be initiated. To incoordinate changes in tissue tension, therefore, as well as to alterations in the calibre of the bloodyessels, he attributes the protean manifestations of the common disorder, to which I have tried to direct professional attention.

In conclusion, it may be said that confirmation of the general view here expressed is also afforded both by the successes and by the failures of treatment; a subject which I reserve for a future communication.

1525 WALNUT STREET.

